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Access DB# 68910

## SEARCH REQUEST FORM

**Scientific and Technical-Information Center**

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 6/17/02  
 Art Unit: 1621 Phone Number 308.4519 Serial Number: 091529.319  
 Mail Box and Bldg/Room Location: CM 7A07 Results Format Preferred (circle): PAPER DISK E-MAIL  
VE12

**If more than one search is submitted, please prioritize searches in order of need.**

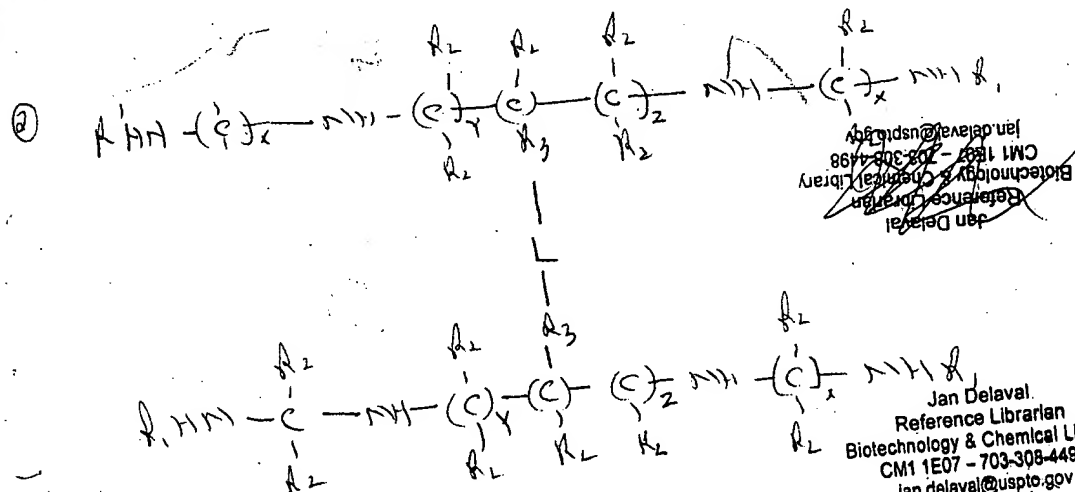
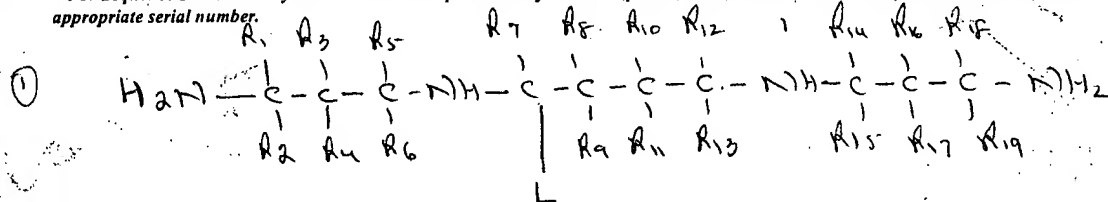
Please provide a detailed statement of the search topic; and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Polyamine Transport Inhibitors.

Inventors (please provide full names): Richard Poulin et al

Earliest Priority Filing Date: \_\_\_\_\_

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



See claims 24, 32, 34, 36, 38

**STAFF USE ONLY**

**Type of Search:**

**Vendors and cost where applicable**

Searcher: \_\_\_\_\_

NA Sequence (#)

STN™

Searcher Phone #: 4498

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Date Searcher Picked Up: 4/1/02

### Bibliographic

**Dr.Link**

Date Completed: 7.1.02

## Litigation

Lexis/Nexis

Searcher Prep & Review Time: \_\_\_\_\_

Fulltext

## Sequence Systems

Clerical Prep Time: 45

### Patent Family

WWW/Internet

Online Time: 5:49

Other

Other (specify):

PTO-1590 (8-01)

Jan Delaval  
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Biotechnology & Chemical Library  
CM1 1E97 - 202-305-4498  
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FILE COVERS 1907 - 1 Jul 2002 VOL 137 ISS 1  
FILE LAST UPDATED: 30 Jun 2002 (20020630/ED)

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L119 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:401776 HCAPLUS

DN 133:38223

TI **Polyamine amide derivative transport inhibitors**, their preparation, and their therapeutic and diagnostic use

IN **Poulin, Richard; Audette, Marie; Charest-Gaudreault, Rene**

PA Universite Laval, Can.; Ilex Oncology, Inc.

SO PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C237-10

ICS C07C323-41; A61K031-16

CC 1-6 (Pharmacology)

Section cross-reference(s): 9, 23, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000034226	A1	20000615	WO 1998-US26493	19981210 <--
	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9919988	A1	20000626	AU 1999-19988	19981210 <--
PRAI	WO 1998-US26493	A	19981210 <--		
OS	MARPAT 133:38223				
AB	The application discloses synthetic derivs. of original <b>polyamines</b>				

in which a carbon atom to the original **polyamine** comprises an amide group **inhibits** the cellular uptake of a natural **polyamine** by specifically binding a cellular **transporter** for a natural **polyamine**. The synthetic derivs. are used to **inhibit** the activity of a natural **polyamine transporter** in the treatment of disorders involving unrestrained cell proliferation and/or differentiation where control of **polyamine transport** is required When used in combination with an **inhibitor** of **polyamine** synthesis.

- ST **polyamine** amide deriv prepn **transport inhibition**; cell proliferation disorder **polyamine** amide deriv; differentiation cell disorder **polyamine** amide deriv
- IT Amines, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(diamines, **transport**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Antitumor agents  
(mammary gland, ZR-75-1; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Mammary gland  
(neoplasm, ZR-75-1, diamine and **polyamine transport** in; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Mammary gland  
Mammary gland  
(neoplasm, **inhibitors**, ZR-75-1; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Amide group  
Cell differentiation  
Cell proliferation  
Cytotoxic agents  
Diagnosis  
Drug delivery systems  
(**polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT **Biological transport**  
(**polyamine transporter**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Amines, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(**polyamines**, nonpolymeric; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT **Proliferation inhibition**  
(proliferation **inhibitors**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT Structure-activity relationship  
(**transport-affecting**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT **Biological transport**  
(uptake; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)
- IT 71-44-3, Spermine  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

## PROC (Process)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 56-18-8, Norspermidine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 206760-63-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 189076-31-1P 206760-64-7P 206760-65-8P 206760-66-9P  
247187-67-3P 247187-68-4P 275353-77-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 70052-12-9, .alpha.-Difluoromethylornithine 206760-67-0  
206760-68-1 206760-69-2 206760-70-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 110-60-1, Putrescine 124-20-9, Spermidine

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

IT 119798-07-1P 186002-24-4P 206760-72-7P 213131-55-6P 244033-31-6P  
275353-76-9P 275353-78-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction; polyamine amide deriv.  
transport inhibitor prepn. and diagnostic and  
therapeutic use)

IT 56-17-7, Cystamine dihydrochloride 76-83-5, Trityl chloride 623-24-5  
22834-83-9, Ornithine hydrochloride 24424-99-5, Di-tert-butyl  
dicarbonate 275353-75-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; polyamine amide deriv. transport  
inhibitor prepn. and diagnostic and therapeutic use)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

(1) Audette, M; WO 9817623 A 1998 HCAPLUS

(2) Hubert, M; Journal of Biological Chemistry 1996, V271(44), P27556

IT 206760-63-6P

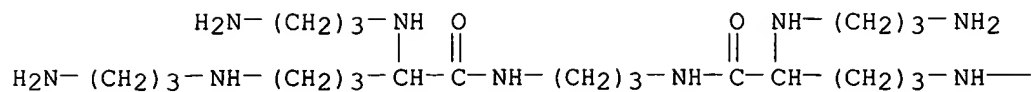
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(polyamine amide deriv. transport inhibitor  
prepn. and diagnostic and therapeutic use)

RN 206760-63-6 HCAPLUS



PAGE 1-A



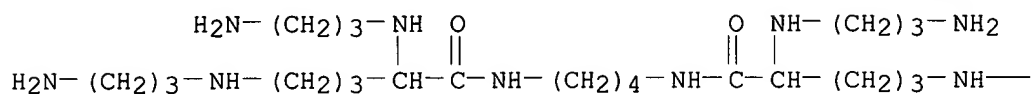
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-68-1 HCAPLUS

CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



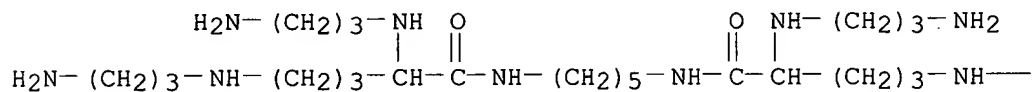
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-69-2 HCAPLUS

CN Pentanamide, N,N'-1,5-pentanediybis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



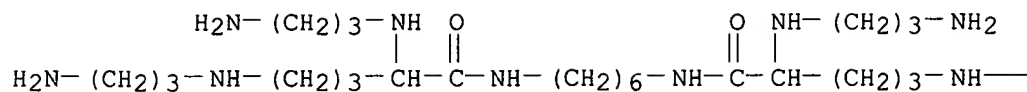
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-70-5 HCAPLUS

CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

L119 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:367983 HCAPLUS

DN 133:22412

TI Cationic lipids for use liposomes for drug delivery

IN Xiang, Gao

PA Vanderbilt University, USA

SO PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A01N033-12

ICS A01N037-18; C07C225-00; C07C233-00; C07D265-30

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 3, 23

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000030444	A1	20000602	WO 1999-US27841	19991123 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 1998-109950P	P	19981125	<--	
	US 1998-110970P	P	19981204	<--	
OS	MARPAT 133:22412				
AB	The present invention relates to synthetic cationic lipids, liposome formulations and the use of such compds. to introduce functional bioactive agents into cultured cells.				
ST	liposome drug delivery cationic lipid				
IT	Gene therapy				
	Transformation, genetic				
	(cationic lipids for use liposomes for drug delivery)				
IT	Ionomers				
	Polyamides, biological studies				
	RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(cationic lipids in liposomes for drug delivery)				
IT	Lipids, biological studies				
	RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(cationic; cationic lipids for use liposomes for drug delivery)				
IT	Drug delivery systems				
	(liposomes, cationic; cationic lipids for use liposomes for drug delivery)				
IT	Polyamines				
	Polyamines				
	RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological				

study); PREP (Preparation); USES (Uses)  
 (polyamide-; cationic lipids in liposomes for drug delivery)

IT Polyamides, biological studies  
 Polyamides, biological studies  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (polyamine-; cationic lipids in liposomes for drug delivery)

IT 279674-76-9P 279674-81-6P 279675-37-5P 284491-03-8P 284491-49-2P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (cationic lipids in liposomes for drug delivery)

IT 272462-70-1P 272462-71-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (pren. and reactions of; cationic lipids for use liposomes for drug delivery)

IT 272462-76-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. and reactions of; cationic lipids for use liposomes for drug delivery)

IT 272462-66-5P 272462-67-6P 272462-68-7P 272462-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and reactions of; cationic lipids for use liposomes for drug delivery)

IT 272462-72-3 **272462-73-4**  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prepn. of; cationic lipids for use liposomes for drug delivery)

IT 57-88-5DP, Cholesterol, conjugates with polyethyleneimine 13055-09-9P  
 15337-57-2P 89101-38-2P 117458-00-1P 134925-48-7P 179075-30-0P  
 179075-31-1P 197974-80-4P 200182-20-3P 209396-83-8P 272462-77-8P  
 272462-79-0P 272462-80-3P 272462-81-4P 272462-82-5P 272462-83-6P  
 272462-84-7P 272462-85-8P 272462-86-9P 272462-87-0P 272462-88-1P  
 272462-89-2P 272462-90-5P 272462-91-6P 272462-92-7P 272462-93-8P  
 272462-94-9P 272462-95-0P 272462-96-1P 272462-97-2P 272462-98-3P  
 272462-99-4P 272463-00-0P 272463-01-1P 272463-02-2P 272463-03-3P  
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 272463-47-5P 272463-48-6P 272463-49-7P 272463-50-0P 272463-51-1P  
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 272463-57-7P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of; cationic lipids for use liposomes for drug delivery)

IT 98-88-4, Benzoyl chloride 102-71-6, reactions 107-13-1,  
 2-Propenenitrile, reactions 110-91-8, Morpholine, reactions 112-77-6,  
 Oleic acid chloride 112-99-2, Dioctadecylamine 123-46-6 540-51-2,  
 2-Bromoethanol 566-88-1, 5.alpha.-Cholestan-3-one 598-21-0,  
 Bromoacetyl bromide 616-30-8, (.+.-)-3-Amino-1,2-propanediol 623-57-4  
 2442-61-7, 1,2-Dioleoylglycerol 3464-50-4, Cholesteryl chloroacetate  
 6110-53-8, Oleyl bromide 6425-32-7 13242-44-9, 2-  
 Dimethylaminoethanethiol hydrochloride 15337-59-4 30189-36-7  
 30734-81-7 35709-09-2, Oleyl mesylate 272462-74-5 272462-75-6  
 272462-78-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)



(reactions of; cationic lipids for use liposomes for drug delivery)  
 RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Lerouge; Chem Phys Lipids 1988

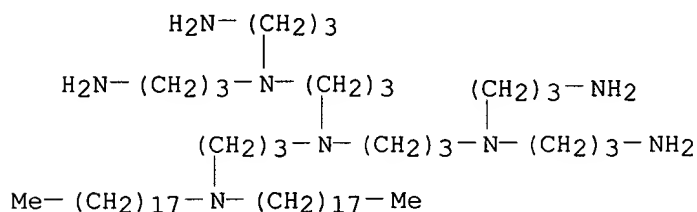
IT 272462-73-4

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of; cationic lipids for use liposomes for drug delivery)

RN 272462-73-4 HCAPLUS

CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(dioctadecylamino)propyl]- (9CI) (CA INDEX NAME)



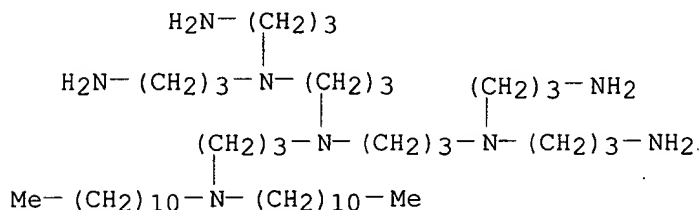
IT 272463-38-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of; cationic lipids for use liposomes for drug delivery)

RN 272463-38-4 HCAPLUS

CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(diundecylamino)propyl]- (9CI) (CA INDEX NAME)



L119 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:335366 HCAPLUS

DN 132:334312

TI synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells

IN Chu, Yongliang; Masoud, Malek; Gebeyehu, Gulilat

PA Life Technologies, Inc., USA

SO PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C211-64

ICS C07C211-63; C07C229-26; C07C211-21; A61K031-14

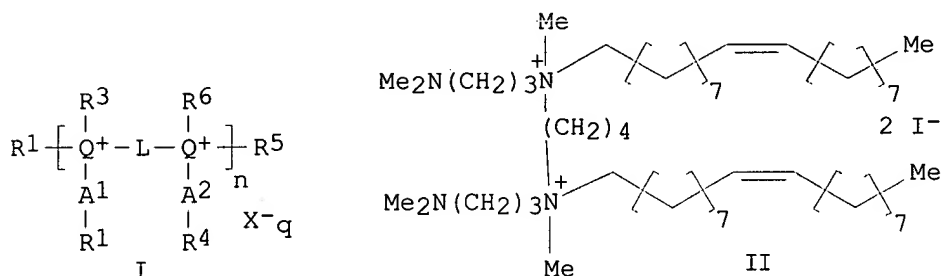
CC 26-3 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 3, 35, 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2000027795 A1 20000518 WO 1999-US26825 19991112 <--  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,  
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1129064 A1 20010905 EP 1999-971794 19991112 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 PRAI US 1998-108117P P 19981112 <--  
 WO 1999-US26825 W 19991112  
 OS MARPAT 132:334312  
 GI



AB Synthesis and activity of transfection reagents (I) [Q = N, O, S; L = (un)substituted alkyl, ether, polyether, amide, polyamide, ester, sulfide, urea, thiourea, guanidyl, carbamoyl, carbonate, phosphate, sulfate, sulfoxide, imine, carbonyl, secondary amine; R1-R6 independently = (un)substituted alkyl, alkenyl, aryl, ether; A1, A2 independently = CH2O, CH2S, CH2NH, CO, C=NH, CS, alkyl; X = physiol. acceptable anion; n = 1-1000; q = no. of pos. charge divided by valence of anion], cationic lipids capable of facilitating **transport** of biol. active agents or substances into cells, are disclosed. Thus, I [R1, R4 = oleyl; R2, R5 = Me2N(CH2)3; R3, R6 = Me; A1, A2 = CH2; L = (CH2)4; X = I] (II) is prep'd. by reaction of bis-1,4-oleyl-1,4-butanediamine with acrylonitrile followed by redn. of nitrile to amine and quaternization of amine with Me iodide. II shows an activity of 37.8 ng/.beta.gal/cm2 in DNA delivery. Formulations contg. I are given.

ST cationic lipid prepn transfection reagent; DNA delivery gene therapy

IT Lipids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polar, cationic; synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)

IT Gene therapy

Transformation, genetic

(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)

IT DNA,

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(synthesis and activity of transfection reagents for **transport**

of biol. active agents or substances into cells)

IT 268539-52-2P 268539-53-3P 268539-54-4P 268539-55-5P  
 268539-56-6P 268539-57-7P 268539-58-8P 268539-59-9P  
 268539-60-2P 268539-61-3P 268539-62-4P 268539-63-5P  
 268554-12-7P 268554-14-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (synthesis and activity of transfection reagents for transport  
 of biol. active agents or substances into cells)

IT 50-99-7, Glucose, reactions 57-48-7, D-Fructose, reactions 57-50-1,  
 reactions 59-23-4, Galactose, reactions 63-42-3, Lactose 69-79-4,  
 Maltose 107-13-1, 2-Propenenitrile, reactions 110-60-1,  
 1,4-Diaminobutane 112-77-6, Oleoyl chloride 528-50-7, Cellobiose  
 3458-28-4, Mannose 4023-02-3 5455-98-1 213131-55-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis and activity of transfection reagents for transport  
 of biol. active agents or substances into cells)

IT 268539-45-3P 268539-46-4P 268539-47-5P 268539-48-6P 268539-49-7P  
 268539-50-0P 268539-51-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthesis and activity of transfection reagents for transport  
 of biol. active agents or substances into cells)

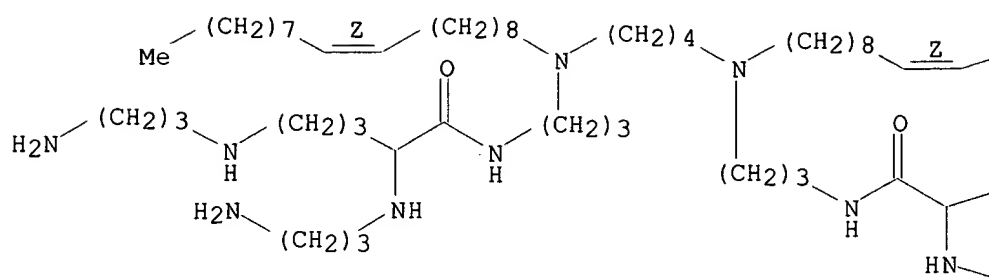
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Can; WO 9840499 A 1998 HCAPLUS  
 (2) Gebeyehu, G; US 5334761 A 1994 HCAPLUS  
 (3) Genzyme Corporation; WO 9802190 A 1998 HCAPLUS  
 (4) Haces, A; US 5674908 A 1997 HCAPLUS  
 (5) Haces, A; WO 9742819 A 1997 HCAPLUS  
 (6) Henkel Und Cie G M B H; FR 1567214 A 1969 HCAPLUS  
 (7) La Roche, H; EP 0846680 A 1998 HCAPLUS  
 (8) Life Technologies Inc; WO 9840502 A 1998 HCAPLUS  
 (9) McCluskie, M; ANTISENSE NUCLEIC ACID DRUG DEV 1998, V8(5), P401 HCAPLUS  
 (10) McCluskie, M; Direct gene transfer to the respiratory tract of mice with  
 pure plasmid and lipid-formulated DNA 1999, V130(8) HCAPLUS  
 (11) Shen, D; US 5830430 A 1998 HCAPLUS  
 (12) Smithkline Beecham Plc; WO 9929712 A 1999 HCAPLUS  
 (13) Wolff, J; US 5744335 A 1998 HCAPLUS

IT 268539-53-3P 268539-54-4P 268539-58-8P  
 268554-12-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (synthesis and activity of transfection reagents for transport  
 of biol. active agents or substances into cells)

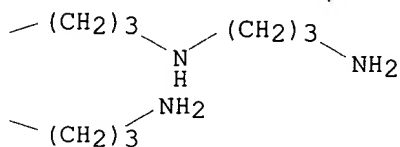
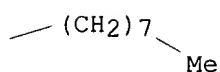
RN 268539-53-3 HCAPLUS  
 CN Pentanamide, N,N'-[1,4-butanediylbis[[ (9Z)-9-octadecenylimino]-3,1-  
 propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

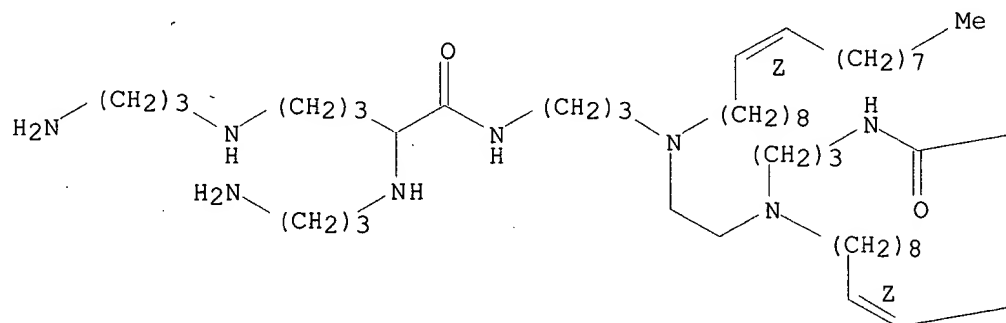


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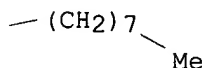
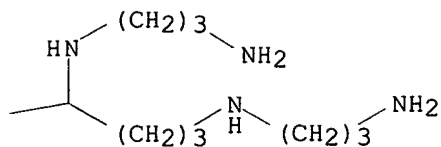
CN Pentanamide, N,N'-[1,2-ethanediylbis[[ (9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



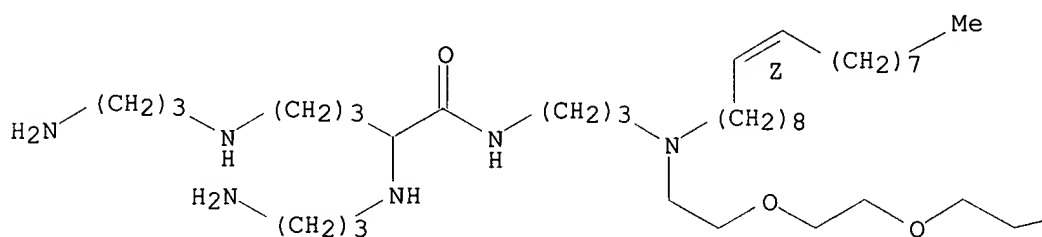
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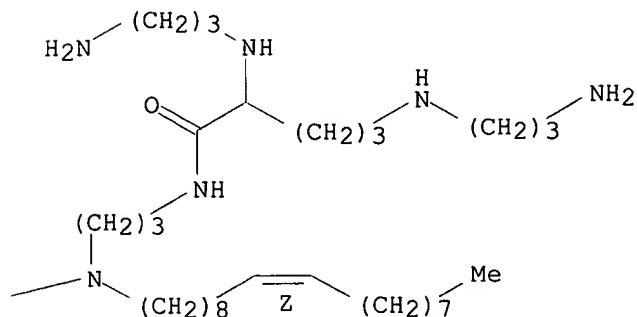
RN 268539-58-8 HCAPLUS  
 CN Pentanamide, N,N'-[4,13-di-(9Z)-9-octadecenyl-7,10-dioxa-4,13-diazahexadecane-1,16-diyl]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



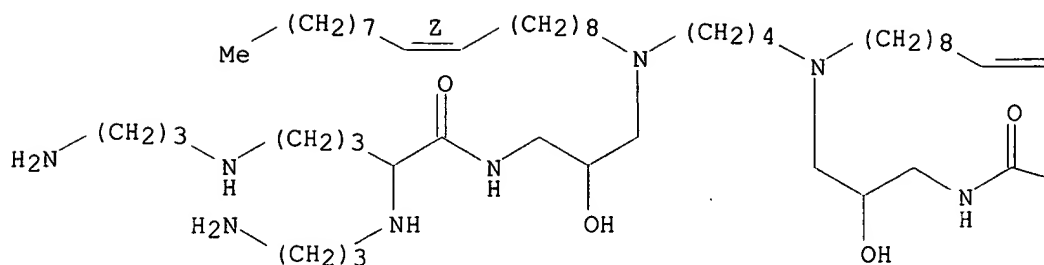
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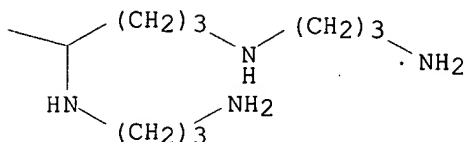
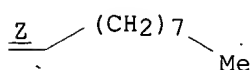
RN 268554-12-7 HCAPLUS  
 CN Pentanamide, N,N'-[1,4-butanediylbis[[ (9Z)-9-octadecenylimino] (2-hydroxy-3,1-propanediyl)]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L119 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:78926 HCAPLUS

DN 132:122935

TI Preparation of amide-based cationic lipids

IN Schwartz, David Aaron; Daily, William J.; Dwyer, Brian Patrick;  
Srinivasan, Kumar; Brown, Bob Dale

PA Genta, Incorporated, USA

SO U.S., 25 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM C07C233-05

NCL 564153000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 3, 63

FAN.CNT 1

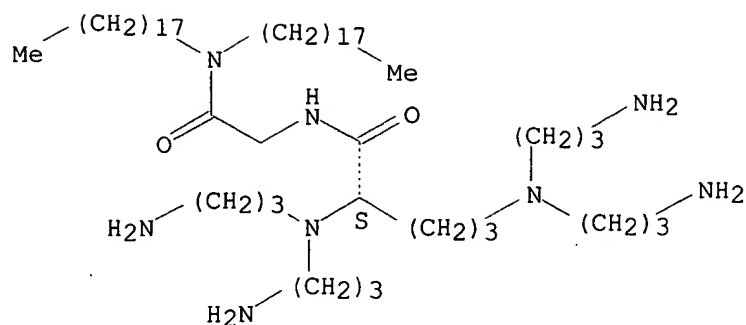
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PI	US 6020526	A	20000201	US 1996-681297	19960722 <--
	US 6339173	B1	20020115	US 1999-327392	19990607 <--
PRAI	US 1996-681297	A1	19960722	<--	

AB Amide-based cationic lipids R<sub>2</sub>(NHCHR<sub>4</sub>CO)<sub>n</sub>(NHCHR<sub>3</sub>)<sub>p</sub>YCOR<sub>1</sub> [X-]<sub>m</sub> (Y = bond, alkylene; R<sub>1</sub> = H, lipophilic moiety; R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> = pos. charged moiety or H, alkyl, heterocyclyl; n, p = 0-8; X- = anion or polyanion; m = integer from zero to a no. equiv. to the pos. charge present on the lipid) or their salts, solvates, or enantiomers were prepd. The present invention further provides compns. of these lipids with polyanionic macromols., methods for interfering with protein expression in a cell utilizing these compns. and a kit for prepg. the same. Thus, N<sub>2</sub>-[N<sub>2</sub>,N<sub>5</sub>-bis(3-aminopropyl)-L-ornithyl]-N,N-diocetadecyl-L-glutamine tetrahydrochloride (I) was prepd. via coupling of N<sub>2</sub>,N<sub>5</sub>-bis[(1,1-dimethylethoxy)carbonyl]-N<sub>2</sub>,N<sub>5</sub>-bis[3-[(1,1-dimethylethoxy)carbonyl]aminopropyl]-L-ornithine N-hydroxysuccinimidyl ester with N,N-diocetadecyl-L-glutamine benzyl ester hydrotrifluoroacetate,

followed by hydrogenolysis over Pd/C and deprotection using HCl in dioxane. The synthesized cationic lipids, including I, were assayed for transient transfection efficiency in COS-7, SNB-19, RD and C8161 cells and for nuclear delivery of oligonucleotides of varying charge densities.

ST peptide amide cationic lipid prepn transfection  
 IT Transformation, genetic  
     (prepn. of amide-based cationic lipids)  
 IT Peptides, preparation  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
     (prepn. of amide-based cationic lipids)  
 IT Lipids, biological studies  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (prepn. of amide-based cationic lipids)  
 IT 176021-45-7P 187978-83-2P 187978-84-3P 187978-86-5P 187978-87-6P  
 187978-96-7P 187979-12-0P 187979-13-1P 187979-20-0P 187979-21-1P  
 187979-29-9P 187979-37-9P 187979-38-0P 187979-39-1P 187979-40-4P  
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
     (prepn. of amide-based cationic lipids)  
 IT 112-99-2P, Dioctadecylamine 504-53-0P, Stearone 556-50-3P,  
 Glycylglycine 1947-00-8P 2566-19-0P 6136-90-9P, 18-  
 Pentatriacontanone, oxime 7536-58-5P 13574-13-5P 30924-93-7P  
 36243-55-7P, 18-Pentatriacontanamine 119798-08-2P 124050-79-9P  
 159684-91-0P 187978-89-8P 187978-90-1P 187978-92-3P 187978-93-4P  
 187978-97-8P 187979-00-6P 187979-02-8P 187979-03-9P 187979-04-0P  
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 187979-18-6P 187979-19-7P 187979-22-2P 187979-23-3P 187979-25-5P  
 187979-26-6P 187979-27-7P 187979-30-2P 187979-32-4P  
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
     (prepn. of amide-based cationic lipids)  
 RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Anon; WO 9601841 1996 HCAPLUS  
 (2) Beher; US 5171678 1992 HCAPLUS  
 (3) Eelgner; US 5264618 1993 HCAPLUS  
 (4) Eppstein; US 4897355 1990  
 (5) Felgner; Proc Natl Acad Sci USA 1987, V84, P7413 HCAPLUS  
 (6) Gebeyehu; US 5334761 1994 HCAPLUS  
 (7) Remy; Bioconjugate chem 1994, V5, P647 HCAPLUS  
 IT **219304-01-5P**  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
     (prepn. of amide-based cationic lipids)  
 RN 219304-01-5 HCAPLUS  
 CN Glycinamide, N2,N2,N5,N5-tetrakis(3-aminopropyl)-L-ornithyl-N,N-dioctadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L119 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:691066 HCAPLUS

DN 131:307091

TI **Polyamine transport inhibitors, their preparation, and their therapeutic use**

IN **Poulin, Richard; Audette, Marie;**

**Charest-Gaudreault, Rene**

PA Universite Laval, Can.; Ilex Oncology, Inc.

SO PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C237-10

ICS C07C211-14; C07C323-41; A61K031-16; A61K031-13

CC 1-6 (Pharmacology)

Section cross-reference(s): 23, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9954283	A1	19991028	WO 1998-US7806	19980421 <--
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	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
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	AU 9871316	A1	19991108	AU 1998-71316	19980421 <--
	EP 1003715	A1	20000531	EP 1998-918385	19980421 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRAI WO 1998-US7806 A 19980421 <--

OS MARPAT 131:307091

AB The invention describes the design, synthesis and therapeutic use of a variety of novel **inhibitors of polyamine transport**. The main feature of this class of **transport inhibitors** is to incorporate a linker or side chain that prevents the uptake of **polyamines** and helps to conjugate **polyamine** analogs to form dimers with high **inhibitory** potency against **polyamine** uptake. These new compds. incorporate features that are designed to maximize their chem. and metabolic stability and their ability to bind to the **polyamine transporter**, and to minimize their toxicity by preventing their absorption by the cells. The purpose of such **inhibitors** is to prevent the uptake or salvaging of circulating **polyamines** by rapidly proliferating cells such as tumor cells, in order to potentiate the effect of

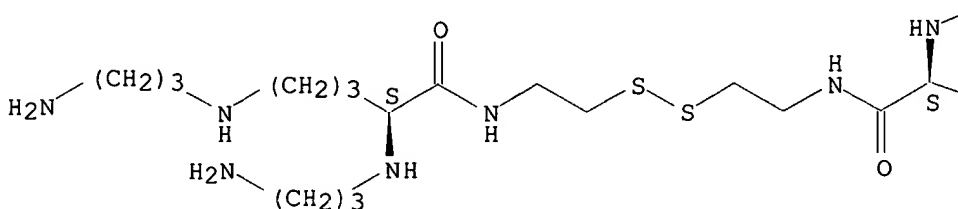


- therapeutic inhibitors of polyamine biosynthesis such as .alpha.-difluoromethylornithene.
- ST polyamine transport inhibitor prepn  
therapeutic; antitumor polyamine transport inhibitor prepn
- IT Affinity labeling  
(affinity ligands; polyamine transport inhibitor prepn. and therapeutic use)
- IT Antitumor agents  
(mammary gland, ZR-75-1; polyamine transport inhibitor prepn. and therapeutic use)
- IT Mammary gland  
(neoplasm, ZR-75-1; polyamine transport inhibitor prepn. and therapeutic use)
- IT Mammary gland  
Mammary gland  
(neoplasm, inhibitors, ZR-75-1; polyamine transport inhibitor prepn. and therapeutic use)
- IT Biological transport  
Cell differentiation  
Cytotoxic agents  
Diagnosis  
Drug delivery systems  
Drug interactions  
(polyamine transport inhibitor prepn. and therapeutic use)
- IT Metabolism  
(polyamine; polyamine transport inhibitor prepn. and therapeutic use)
- IT Amines, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(polyamines, nonpolymeric; polyamine transport inhibitor prepn. and therapeutic use)
- IT Proliferation inhibition  
(proliferation inhibitors; polyamine transport inhibitor prepn. and therapeutic use)
- IT Structure-activity relationship  
(spermine transport-inhibitory; polyamine transport inhibitor prepn. and therapeutic use)
- IT Biological transport  
(uptake; polyamine transport inhibitor prepn. and therapeutic use)
- IT 79-17-4, Aminoguanidine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(polyamine transport inhibitor prepn. and therapeutic use)
- IT 184895-97-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(polyamine transport inhibitor prepn. and therapeutic use)
- IT 184895-98-5P 184895-99-6P 184896-08-0P 189076-31-1P  
247187-66-2P 247187-67-3P 247187-68-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(polyamine transport inhibitor prepn. and

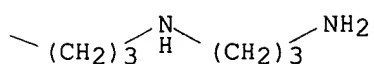
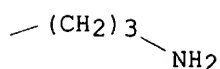
- therapeutic use)
- IT 71-44-3D, Spermine, derivs. 110-60-1D, Putrescine, derivs. 124-20-9D, Spermidine, derivs. 70052-12-9, .alpha.-Difluoromethylornithine 184896-00-2 184896-01-3 184896-02-4 206760-70-5 247187-63-9 247187-64-0 247187-65-1  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (polyamine transport inhibitor prepn. and therapeutic use)
- IT 71-44-3, Spermine 110-60-1, 1,4-Butanediamine 124-20-9, Spermidine 9001-53-0, Copper amine oxidase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (polyamine transport inhibitor prepn. and therapeutic use)
- IT 119798-07-1P 119798-08-2P 124076-28-4P 184896-06-8P 184896-07-9P 244033-31-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and reaction; polyamine transport inhibitor prepn. and therapeutic use)
- IT 56-17-7, Cystamine dihydrochloride 56-18-8, Norspermidine 70-26-8, Ornithine 76-83-5, Trityl chloride 107-13-1, 2-Propenenitrile, reactions 623-24-5, .alpha.,.alpha.'-Dibromo-p-xylene 24424-99-5, Di-tert-butyl dicarbonate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction; polyamine transport inhibitor prepn. and therapeutic use)
- RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
- (1) Ask, A; Cancer Letters 1993, V69, P33 HCAPLUS
  - (2) Audette, M; WO 9817623 A 1998 HCAPLUS
  - (3) Aziz, K; Journal of Pharmacology and Experimental Therapeutics 1995, V274(1), P181
  - (4) Aziz, S; US 5456908 A 1995 HCAPLUS
  - (5) Hubert, M; Journal of Biological Chemistry 1996, V271(44), P27556
  - (6) Univ New York; WO 9312777 A 1993 HCAPLUS
- IT 184895-97-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (polyamine transport inhibitor prepn. and therapeutic use)
- RN 184895-97-4 HCAPLUS
- CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

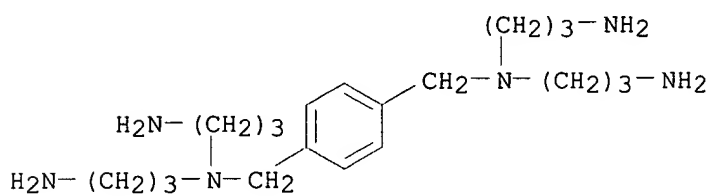


IT 189076-31-1P 247187-66-2P 247187-67-3P

RL: **BAC** (Biological activity or effector, except adverse); **BSU**  
 (Biological study, unclassified); **SPN** (Synthetic preparation); **THU**  
 (Therapeutic use); **BIOL** (Biological study); **PREP**  
 (Preparation); **USES** (Uses)  
 (polyamine transport inhibitor prepn. and  
 therapeutic use)

RN 189076-31-1 HCAPLUS

CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA  
 INDEX NAME)

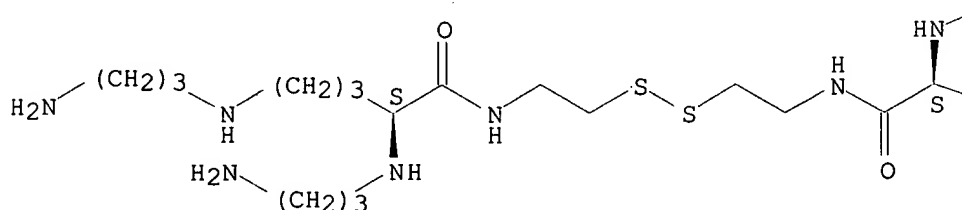


RN 247187-66-2 HCAPLUS

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-  
 aminopropyl)amino]-, octahydrochloride, (2S,2'S)- (9CI) (CA INDEX NAME)

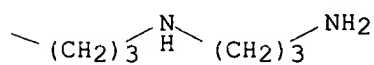
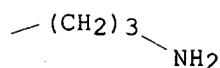
Absolute stereochemistry.

PAGE 1-A

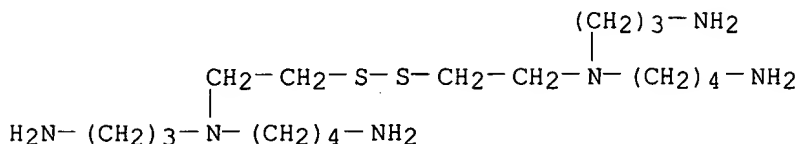


● 8 HCl

PAGE 1-B



RN 247187-67-3 HCAPLUS  
 CN 1,4-Butanediamine, N,N'-(dithiodi-2,1-ethanediyl)bis[N-(3-aminopropyl)-  
 (9CI) (CA INDEX NAME)

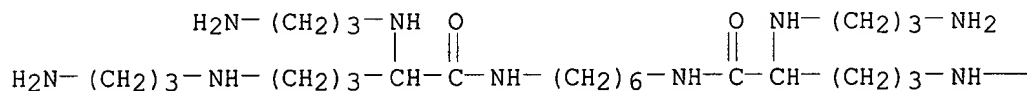


IT 206760-70-5 247187-63-9 247187-64-0  
 247187-65-1

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (polyamine transport inhibitor prepn. and  
 therapeutic use)

RN 206760-70-5 HCAPLUS  
 CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
 (CA INDEX NAME)

PAGE 1-A



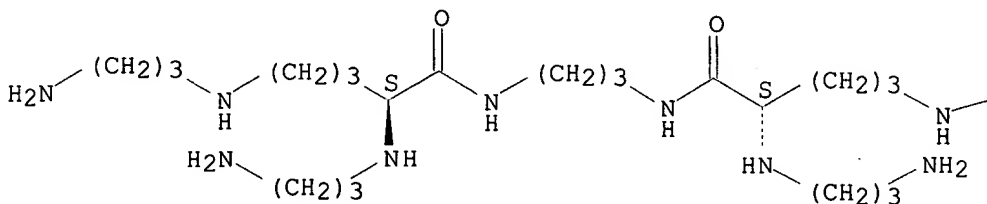
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>-NH<sub>2</sub>

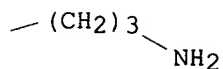
RN 247187-63-9 HCAPLUS  
 CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]-,  
 (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



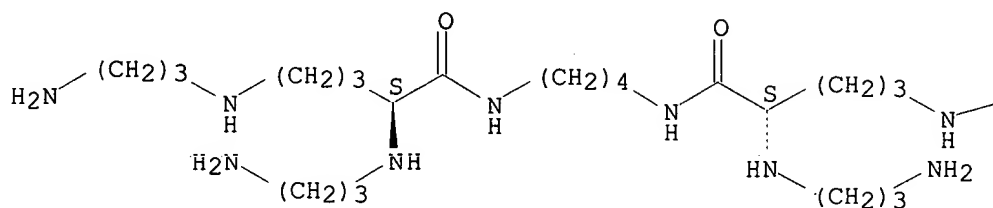
PAGE 1-B



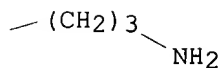
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 CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]-,  
 (2S,2'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



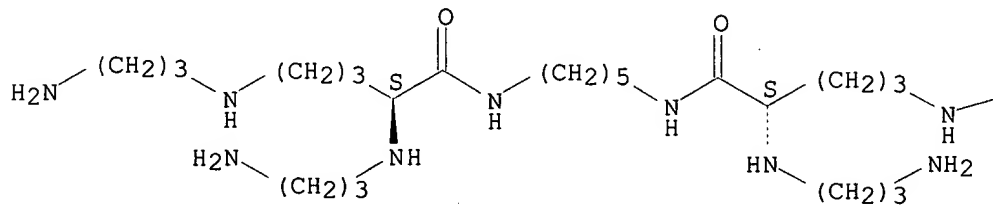
PAGE 1-B



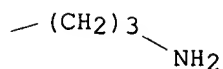
RN 247187-65-1 HCAPLUS  
 CN Pentanamide, N,N'-1,5-pentanediylylbis[2,5-bis[(3-aminopropyl)amino]-,  
 (2S,2'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AN 1999:404110 HCAPLUS  
 DN 131:228866  
 TI Synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**  
 AU Covassin, Laurence; Desjardins, Michel; Charest-Gaudreault, Rene ; Audette, Marie; Bonneau, Marie-Josée; Poulin, Richard  
 CS Faculty of Pharmacy, Laval University, QC, G1K 7P4, Can.  
 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(12), 1709-1714  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 CC 31-6 (Alkaloids)  
 Section cross-reference(s): 1  
 AB A series of novel spermidine and sym-norspermidine dimers was synthesized by crosslinking the polyamine backbones via alkylation of their secondary amino groups to Bu, trans-2-butenyl, 2-butyryl or p-xylyl bridges. The resulting hexamines behaved as high-affinity antagonists of polyamine uptake, with a relative potency that was dependent on the geometry of the linker structure.  
 ST spermidine dimer prepolymer polyamine **transport inhibitor**;  
 norspermidine dimer prepolymer polyamine **transport inhibitor**  
 IT Structure-activity relationship  
 (antitumor; synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 IT Amines, preparation  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (polyamines, nonpolymeric; synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 IT Antitumor agents  
 Biological **transport**  
 (synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 IT 101394-77-8P 201859-92-9P 244033-18-9P  
 244033-19-0P 244033-20-3P 244033-21-4P  
 244033-22-5P 244033-23-6P 244033-24-7P  
 244033-25-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 IT 56-18-8, sym-Norspermidine 110-57-6 124-20-9, Spermidine 543-20-4, Succinyl chloride 623-24-5 821-10-3, 1,4-Dichloro-2-butyne  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 IT 163883-05-4P 244033-13-4P 244033-14-5P 244033-15-6P 244033-16-7P  
 244033-17-8P 244033-26-9P 244033-27-0P 244033-28-1P 244033-29-2P  
 244033-30-5P 244033-31-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)  
 RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Aziz, S; J Pharmacol Exp Ther 1995, V274, P181 HCAPLUS  
 (2) Behr, J; Bioconjugate Chem 1994, V5, P382 HCAPLUS  
 (3) Bergeron, R; Bioinorg Chem 1986, V14, P345 HCAPLUS  
 (4) Brzezinska, E; J Org Chem 1994, V59, P8239 HCAPLUS

- (5) Cheng, Y; Biochem Pharmacol 1973, V22, P3099 HCAPLUS
- (6) Cohen, G; J Chem Soc Chem Commun 1992, P298 HCAPLUS
- (7) Covassin, L; Unpublished results
- (8) Demontigny, D; Unpublished results
- (9) Durantion, B; Cancer Res 1997, V57, P573 HCAPLUS
- (10) Huber, M; J Biol Chem 1996, V271, P27556 HCAPLUS
- (11) Lessard, M; J Biol Chem 1995, V270, P1685 HCAPLUS
- (12) Marton, L; Ann Rev Pharmacol Toxicol 1995, V35, P55 HCAPLUS
- (13) Minchin, R; Biochem J 1989, V262, P391 HCAPLUS
- (14) Porter, C; Cancer Res 1985, V45, P2050 HCAPLUS
- (15) Poulin, R; J Biol Chem 1995, V270, P1695 HCAPLUS
- (16) Seiler, N; Cancer Res 1990, V50, P5077 HCAPLUS
- (17) Seiler, N; Int J Biochem Cell Biol 1996, V28, P843 HCAPLUS
- (18) Simard, J; Endocrinology 1990, V126, P3223 HCAPLUS
- (19) Zang, E; Synth Commun 1997, V27, P3145 HCAPLUS

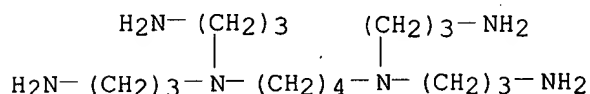
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 244033-19-0P 244033-20-3P 244033-21-4P  
 244033-22-5P 244033-23-6P 244033-24-7P  
 244033-25-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis of spermidine and norspermidine dimers as high affinity polyamine transport inhibitors)

RN 101394-77-8 HCAPLUS

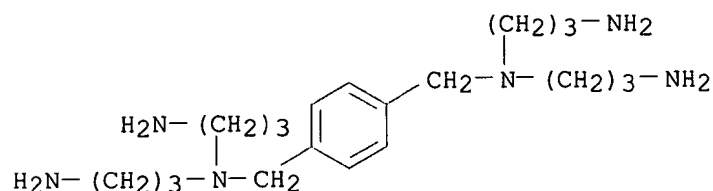
CN 1,4-Butanediamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



● 6 HCl

RN 201859-92-9 HCAPLUS

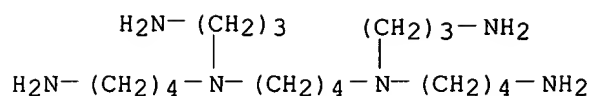
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



● 6 HCl

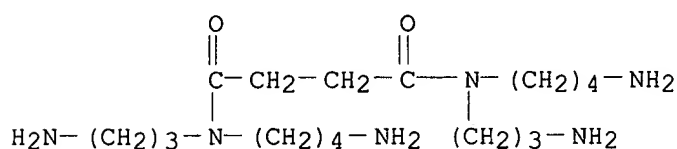
RN 244033-18-9 HCAPLUS

CN 1,4-Butanediamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



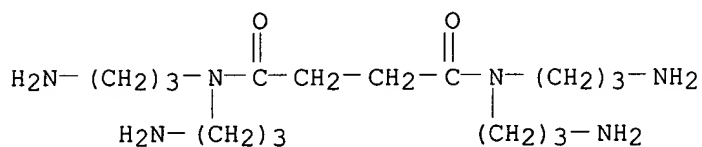
● 6 HCl

RN 244033-19-0 HCAPLUS  
 CN Butanediamide, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

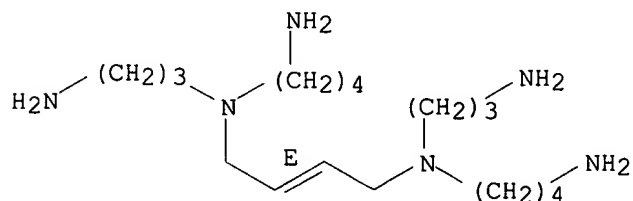
RN 244033-20-3 HCAPLUS  
 CN Butanediamide, N,N,N',N'-tetrakis(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 244033-21-4 HCAPLUS  
 CN 2-Butene-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)

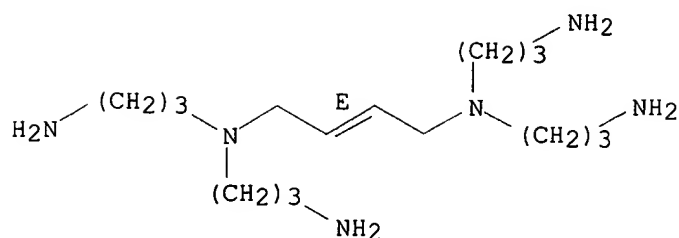
Double bond geometry as shown.



RN 244033-22-5 HCAPLUS  
 CN 2-Butene-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)

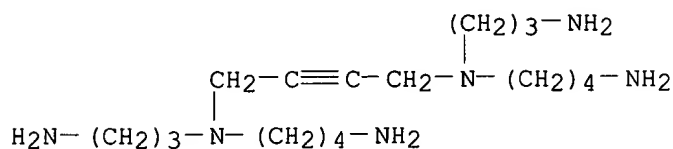
Double bond geometry as shown.





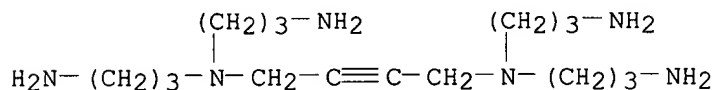
RN 244033-23-6 HCAPLUS

CN 2-Butyne-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-  
(9CI) (CA INDEX NAME)



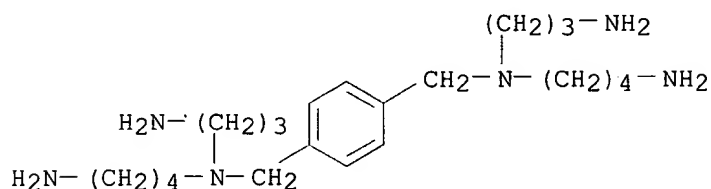
RN 244033-24-7 HCAPLUS

CN 2-Butyne-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)



RN 244033-25-8 HCAPLUS

CN 1,4-Benzenedimethanamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-,  
hexahydrochloride (9CI) (CA INDEX NAME)



● 6 HCl

L119 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:136874 HCAPLUS

DN 130:153974

TI Preparation of novel lipopolyamines and their use in **transport**  
liposomes for carrying transfection agents

IN Klosel, Roland; Konig, Stephan

PA Biontex Laboratories G.m.b.H., Germany

SO PCT Int. Appl., 64 pp.

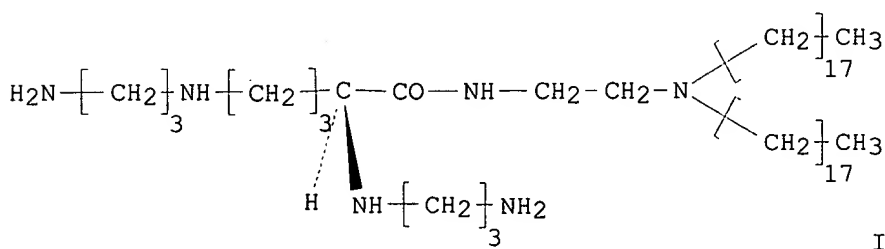
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

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PI	WO 9908997	A1	19990225	WO 1998-EP5156	19980813	<--
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	AU 745958	B2	20020411			
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	JP 2001515060	T2	20010918	JP 2000-509683	19980813	<--
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	ES 2167939	T3	20020516	ES 1998-946333	19980813	<--
	US 6281371	B1	20010828	US 2000-463172	20000329	<--
PRAI	DE 1997-19735125	A	19970813	<--		
	DE 1998-19834683	A	19980731	<--		
	WO 1998-EP5156	W	19980813	<--		
OS	MARPAT 130:153974					
GI						

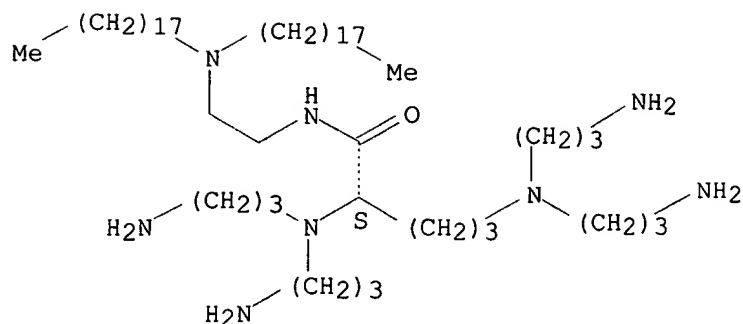


AB The invention relates to novel lipopolyamines [H(NH(CH<sub>2</sub>)<sub>a</sub>)<sub>b</sub>]<sub>2</sub>-  
nN(H)n(CH<sub>2</sub>)<sub>x</sub>(R)(CH<sub>2</sub>)<sub>d</sub>N(H)m([(CH<sub>2</sub>)<sub>e</sub>NH]fH)<sub>2</sub>-m, where R = (CH<sub>2</sub>)<sub>g</sub>N(R<sub>1</sub>)(R<sub>2</sub>);  
R<sub>1</sub>, R<sub>2</sub> = independently (un)satd., (un)substituted alkyl; X = N,  
N(CH<sub>2</sub>)<sub>h</sub>C(O)NH, N(CH<sub>2</sub>)<sub>r</sub>C(O)O, N(CH<sub>2</sub>)<sub>k</sub>NHC(O), N(CH<sub>2</sub>)<sub>k</sub>OC(O), CHC(O)NH,  
CHC(O)O, CHC(O)NH(CH<sub>2</sub>)<sub>l</sub>NH, CHCH<sub>2</sub>NH; [see text for values and combinations  
of letter subscripts], (including their salts), characterized by a sym.,  
highly flexible lipophilic component with a buffering capacity at physiol.  
pH, and to their use for funneling biol. active materials such as DNA,  
RNA, ribozymes, anti-sense DNA, peptides and proteins into eukaryotic  
cells in vivo or in vitro. Thus, N-BOC-N',N'-dioctadecylethylenediamine  
was prepd. from N-BOC-ethylenediamine and octadecyl bromide, and reacted  
with tetra-BOC-carboxyspermine, and the product N-deprotected to give I as  
its tetra-TFA salt. In in vitro transfection tests of  
pCVM<Sport>.beta.-Gal with CV-1, Hela S3, and NIH 3T3 cells, liposomes  
constructed from I and dioleoylphosphatidylethanoamine,  
dioleoylphosphatidylcholine, cholesterol, or cholesteryl-amine, in

presence or absence of serum, showed relative transfection efficiencies of 66-100%.

- ST lipopolyamine prepn octadecylethylenediamine carboxyspermine  
**transport** liposome transfection
- IT Amines, preparation  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(polyamines, nonpolymeric; reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT Transformation, genetic  
(prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT Amino acids, preparation  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT 107-13-1, 2-Propenenitrile, reactions 112-89-0, Octadecyl bromide 3184-13-2, Ornithine hydrochloride 5003-71-4, 3-Bromopropylamine hydrobromide 57260-73-8 119798-08-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT 83948-53-2P 220170-77-4P 220170-78-5P 220170-79-6P 220170-80-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT 220170-83-2P 220170-84-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT 220170-82-1P 220170-86-5P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- IT 220170-85-4 220170-87-6 220170-88-7  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
- (1) Boehringer Mannheim GmbH; EP 0544292 A 1993 HCAPLUS
  - (2) Centre Nat Rech Scient; EP 0394111 A 1990 HCAPLUS
  - (3) Eltz, H; WO 9700241 A 1997 HCAPLUS
  - (4) Life Technologies Inc; WO 9405624 A 1994 HCAPLUS
  - (5) Patrick, D; WO 9703939 A 1997 HCAPLUS
  - (6) Vical Inc; WO 9116024 A 1991
- IT 220170-87-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)
- RN 220170-87-6 HCAPLUS
- CN Pentanamide, 2,5-bis[bis(3-aminopropyl)amino]-N-[2-(dioctadecylamino)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L119 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:414726 HCAPLUS

DN 129:62994

TI Cationic amphiphiles containing amino acid or derivatized amino acid groups for intracellular delivery of therapeutic molecules

IN Harris, David J.; Lee, Edward R.; Siegel, Craig S.; Rowe, Eric A.; Hubbard, Shirley C.

PA Genzyme Corporation, USA

SO U.S., 52 pp., Cont.-in-part of U.S. 5,747,471.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-70

ICS A61K017-28; A61K031-56; A61K048-00; B61F017-28

NCL 514044000

CC 1-12 (Pharmacology)

Section cross-reference(s): 2, 14, 32

FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5767099	A	19980616	US 1995-546086	19951020 <--
	US 5650096	A	19970722	US 1994-352479	19941209 <--
	US 5747471	A	19980505	US 1995-540867	19951011 <--
	AU 9732315	A1	19980417	AU 1997-32315	19970610 <--
	AU 736143	B2	20010726		
	EP 1007003	A1	20000614	EP 1997-927989	19970610 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001500897	T2	20010123	JP 1998-515603	19970610 <--
PRAI	US 1994-352479	A2	19941209	<--	
	US 1995-540867	A2	19951011	<--	
	WO 1997-US9748	W	19970610	<--	

OS MARPAT 129:62994

AB Novel cationic amphiphiles are provided that facilitate **transport** of biol. active (therapeutic) mols. into cells. The amphiphiles contain lipophilic groups derived from steroids and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines, polyalkylamines or amino acids. The products may be used to provide gene therapy and deliver antisense polynucleotides or biol. active polypeptides to cells. For gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation, such as cystic fibrosis. Thus, the carbamate  $\text{H}_2\text{N}(\text{CH}_2)_3\text{NH}(\text{CH}_2)_4\text{N}(\text{COCH}_2\text{NHCO}_2\text{R})(\text{CH}_2)_3\text{NH}_2$  [R = 3-cholesteryl] was prepd. by treating N-tert-butoxycarbonylglycine N-hydroxysuccinimide ester with N1,N12-di-benzyloxycarbonylspermine, benzyloxycarbonylation at N9, de-tert-butoxycarbonylation, reaction with cholesteryl chloroformate, and

deblocking. The product was effective in enhancing cell transfection efficiency.

ST steroid carbamate **polyamine** amino acid prepn; cell transfection  
steroid carbamate; gene therapy steroid carbamate

IT Gene therapy

Transformation, genetic

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179074-99-8 179075-00-4 179075-01-5 179075-02-6 179075-05-9  
179075-07-1 179075-08-2 179075-10-6 179075-11-7 179075-12-8  
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179075-32-2 179075-33-3 179075-34-4 179075-38-8 179075-39-9  
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209112-46-9 209112-47-0 209112-48-1 209112-50-5

RL: BUU (Biological use, unclassified); BIOL (Biological study);

USES (Uses)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-25-3P 179075-30-0P 179075-37-7P 179075-40-2P

RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-04-8P 179075-31-1P 179075-36-6P 179075-41-3P 179075-44-6P  
179075-45-7P 179075-46-8P 179075-47-9P 179075-48-0P 179075-49-1P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 56-18-8, N-(3-Aminopropyl)-1,3-propanediamine 71-44-3, Spermine  
80-97-7, Dihydrocholesterol 112-99-2 143-23-7, Bis(6-aminoethyl)amine  
628-20-6, 4-Chlorobutyronitrile 910-31-6, Cholesteryl chloride  
3392-07-2 4799-67-1, 3-Benzoyloxy-1,2-propanediol 7144-08-3,  
Cholesteryl chloroformate 14611-34-8 20255-94-1, 1,2-  
Dimyristoylglycerol 30189-36-7 51323-71-8, Dodecyl methanesulfonate  
89965-56-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 2206-21-5P 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P  
103493-12-5P 105793-81-5P 149204-03-5P 179075-52-6P 179075-53-7P  
179075-54-8P 179075-55-9P 179075-56-0P 179075-58-2P 179075-59-3P  
179075-62-8P 179075-66-2P 179075-67-3P 179075-68-4P 179075-69-5P  
179075-70-8P 179075-71-9P 179075-72-0P 179075-73-1P 183249-68-5P  
200813-36-1P 202649-06-7P 202649-07-8P 202649-08-9P 209112-59-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-63-9P 179075-74-2P 203917-63-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 209112-50-5

RL: BUU (Biological use, unclassified); BIOL (Biological study);

USES (Uses)

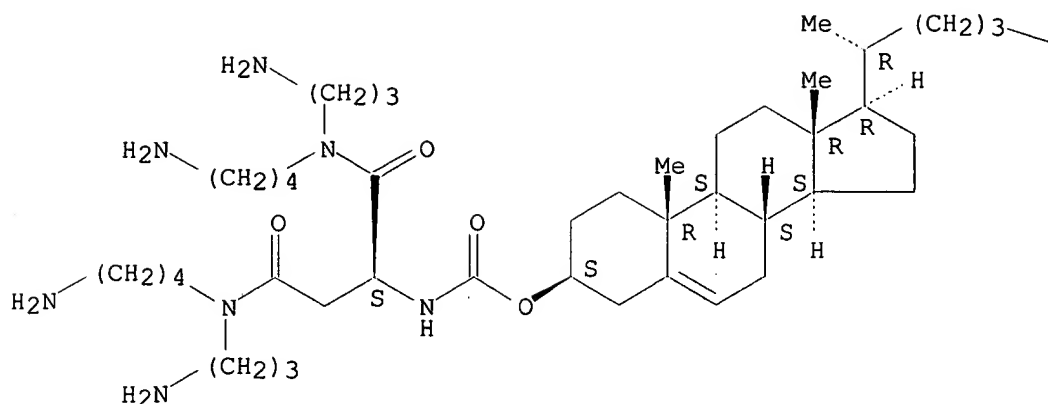
(amphiphilic steroid carbamates for cell transfection and gene therapy)

RN 209112-50-5 HCAPLUS

CN Cholest-5-en-3-ol (3.beta.)-, [(1S)-3-[(4-aminobutyl)(3-aminopropyl)amino]-  
1-[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe<sub>2</sub>

L119 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:282396 HCAPLUS

DN 129:8571

TI Cationic amphiphiles containing steroid lipophilic groups for intracellular delivery of therapeutic molecules

IN Siegel, Craig S.; Harris, David J.; Lee, Edward R.; Hubbard, Shirley C.; Cheng, Seng H.; Eastman, Simon J.; Marshall, John; Scheule, Ronald K.; Lane, Mathieu B.; Rowe, Eric A.

PA Genzyme Corp., USA

SO U.S., 53 pp., Cont.-in-part of U.S. Ser. No. 352,479.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K048-00

ICS A61K031-56; A61K031-70; B01F017-28

NCL 514044000

CC 63-5 (Pharmaceuticals)

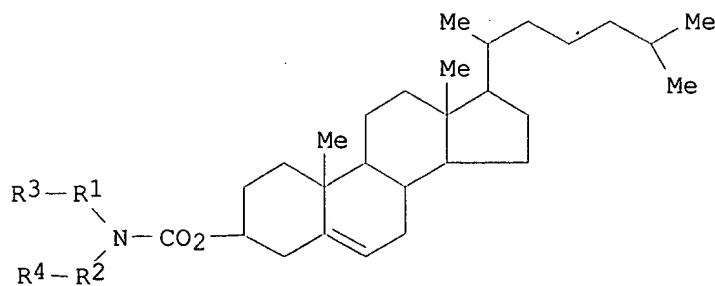
Section cross-reference(s): 32

FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5747471	A	19980505	US 1995-540867	19951011 <--
	US 5650096	A	19970722	US 1994-352479	19941209 <--
	US 6071890	A	20000606	US 1995-545473	19951019 <--
	US 5719131	A	19980217	US 1995-546110	19951020 <--
	US 5767099	A	19980616	US 1995-546086	19951020 <--
	US 5840710	A	19981124	US 1995-546087	19951020 <--
	US 5910487	A	19990608	US 1995-546205	19951020 <--
	CA 2205968	AA	19960620	CA 1995-2205968	19951208 <--
	WO 9618372	A2	19960620	WO 1995-US16174	19951208 <--
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,				

NE, SN, TD, TG

AU 9645161	A1	19960703	AU 1996-45161	19951208	<--
AU 716706	B2	20000302			
EP 799059	A1	19971008	EP 1995-943769	19951208	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
JP 10510813	T2	19981020	JP 1995-519236	19951208	<--
US 5783565	A	19980721	US 1996-595375	19960201	<--
US 5948767	A	19990907	US 1996-679514	19960712	<--
US 5939401	A	19990817	US 1996-680354	19960715	<--
US 6331524	B1	20011218	US 1997-835213	19970407	<--
WO 9813026	A1	19980402	WO 1997-US9748	19970610	<--
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9732315	A1	19980417	AU 1997-32315	19970610	<--
AU 736143	B2	20010726			
EP 1007003	A1	20000614	EP 1997-927989	19970610	<--
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JP 2001500897	T2	20010123	JP 1998-515603	19970610	<--
US 6383814	B1	20020507	US 1999-228232	19990111	<--
AU 734980	B2	20010628	AU 1999-57180	19991101	<--
AU 9957180	A1	20000106			
PRAI US 1994-352479	A2	19941209	<--		
US 1995-4344P	P	19950926	<--		
US 1995-4399P	P	19950927	<--		
US 1995-540867	A2	19951011	<--		
US 1995-545473	A	19951019	<--		
US 1995-546087	A1	19951020	<--		
US 1995-546110	A2	19951020	<--		
US 1995-564087	A1	19951020	<--		
WO 1995-US16174	W	19951208	<--		
US 1996-661279	A2	19960610	<--		
US 1996-667122	B2	19960620	<--		
US 1996-668676	B1	19960625	<--		
WO 1997-US9748	W	19970610	<--		
OS MARPAT 129:8571					
GI					



AB Novel cationic amphiphiles I (R1, R2 = alkylamine, polyalkylamine; R3, R4 = H satd. or unsatd. aliph. group; R1 and R2 may be the same or different) are provided that facilitate **transport** of biol. active (therapeutic) mols. into cells. Thus, N1,N8-dicarbobenzoxy spermidine was treated with cholesteryl chloroformate followed by hydrogenolysis to give N4-spermidine cholesteryl carbamate. The amphiphiles contain lipophilic groups derived from steroids, from mono or dialkylamines, or from ether or ester-linked alkyl groups, and cationic groups, protonatable at physiolo. pH, derived from amines, alkylamines or polyalkylamines. There are provided also therapeutic compns. prepd. typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols.

Therapeutic mols. that can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic compns. of the invention include providing gene therapy, and delivery of antisense polynucleotides or biol. active polypeptides to cells. With respect to therapeutic compns. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation.

ST cationic amphiphile steroid lipophilic group; drug delivery therapeutic cationic amphiphile steroid

IT Drug delivery systems

Gene therapy

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT Steroids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT Peptides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT. **Biological transport**

(drug; cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 179075-25-3P 179075-30-0P 179075-31-1P 179075-32-2P 179075-35-5P  
179075-36-6P 179075-37-7P 179075-40-2P 203917-63-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 179075-00-4 179075-01-5 179075-02-6 179075-04-8 179075-05-9  
179075-07-1 179075-08-2 **179075-09-3** 179075-10-6  
179075-11-7 179075-12-8 179075-13-9 179075-14-0 179075-15-1  
179075-29-7 179075-33-3 179075-34-4 179075-38-8 179075-39-9  
179075-41-3 179075-42-4 179075-43-5 179075-44-6 179075-45-7  
179075-46-8 179075-47-9 179075-48-0 179075-49-1 179075-50-4  
207386-54-7 207386-55-8

RL: **BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use);**

**BIOL (Biological study); USES (Uses)**

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 71-44-3, Spermine 85-41-6, Phthalimide 107-13-1, Acrylonitrile, reactions 112-99-2 910-31-6, Cholesteryl chloride 4799-67-1  
7144-08-3, Cholesteryl chloroformate 14611-34-8 89965-56-0  
179075-73-1 202649-07-8 207386-52-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 80-97-7P, Dihydrocholesterol 628-20-6P, 4-Chlorobutyronitrile  
2206-21-5P 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P  
103493-12-5P 105793-81-5P 179075-53-7P 179075-62-8P 179075-66-2P  
179075-67-3P 179075-68-4P 179075-69-5P 179075-70-8P 179075-71-9P  
179075-72-0P 183249-68-5P 200813-36-1P 202649-06-7P 207386-53-6P

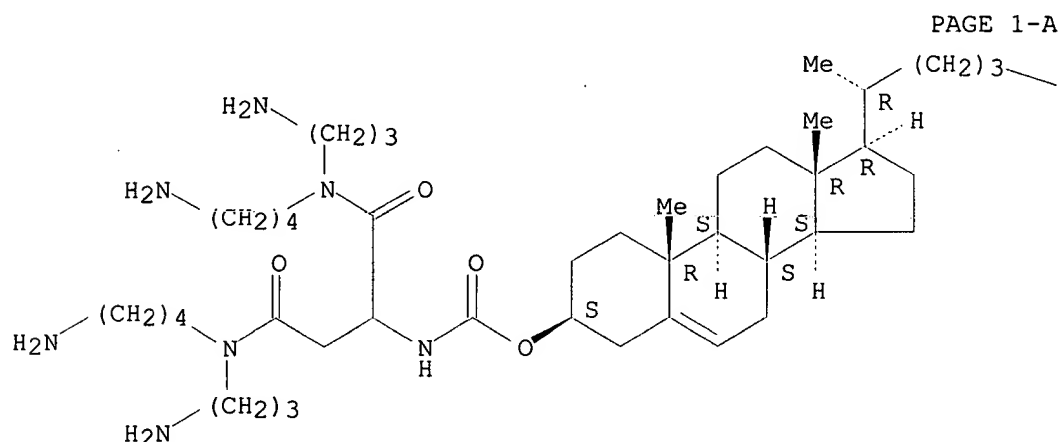
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cationic amphiphiles contg. steroid lipophilic groups for



intracellular delivery of therapeutic mols.)  
 IT 179075-09-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)  
 RN 179075-09-3 HCAPLUS  
 CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe<sub>2</sub>

L119 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1998:268467 HCAPLUS  
 DN 128:321804  
 TI Preparation of spermine analogs for use as polyamine transport inhibitors  
 IN Poulin, Richard; Audette, Marie; Charest-Gaudreault, Rene  
 PA Universite Laval, Can.; Poulin, Richard; Audette, Marie; Charest-Gaudreault, Rene  
 SO PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07C211-13  
 CC 31-6 (Alkaloids)  
 Section cross-reference(s): 1, 34, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817623	A2	19980430	WO 1997-IB1651	19971022 <--
	WO 9817623	A3	19980903		
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,				

LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
 SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG,  
 KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG

US 6083496	A	20000704	US 1996-735130	19961022 <--
CA 2241339	AA	19980430	CA 1997-2241339	19971022 <--
AU 9857752	A1	19980515	AU 1998-57752	19971022 <--
EP 876327	A2	19981111	EP 1997-953991	19971022 <--

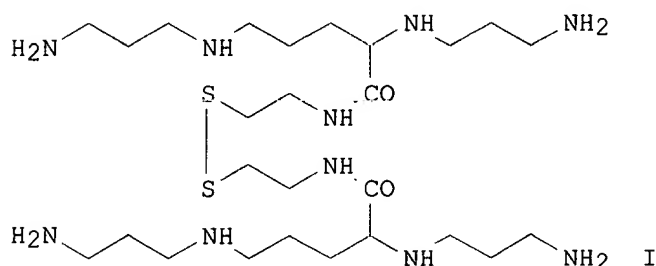
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI

PRAI US 1996-735130 A 19961022 <--

WO 1997-IB1651 W 19971022 <--

OS MARPAT 128:321804

GI



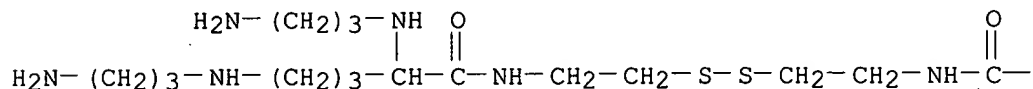
AB Spermine analogs, such as  $R_1NHCR_2R_3(CH_2)_wNH(CH_2)_xCH(CONHR)(CH_2)_yNH(CH_2)_zCR_2R_3NHR_1$  [R = H, moiety which cannot be captured by **polyamine transporter**;  $R_1 = R_2 = R_3 = H$ , alkyl;  $w = 2, 3$ ;  $z = 2, 3$ ;  $x =$  integer from 1 to  $n$ ;  $n =$  integer from 3 to 6;  $yr = n$  minus  $x$ ], were prepd. for therapeutic use as novel **inhibitors of polyamine transport**. The main feature of this class of **transport inhibitors** is to incorporate a linker or side chain that prevents the uptake of **polyamines** and helps to conjugate **polyamine** analogs to form dimers with high **inhibitory** potency against **polyamine** uptake. These new compds. incorporate features that were designed to maximize their chem. and metabolic stability and their ability to bind to the **polyamine transporter**, and to minimize their toxicity by preventing their absorption by the cells. The purpose of such **inhibitors** is to prevent the uptake or salvaging of circulating **polyamines** by rapidly proliferating cells such as tumor cells, in order to potentiate the effect of therapeutic **inhibitors of polyamine** biosynthesis such as Eflornithine. Thus, spermine analog I was prepd. starting from ornithine hydrochloride and cystamine dihydrochloride. Prepd. compds. underwent pharmacol. testing as well as testing to detn. **inhibition of cell proliferation of tumor cell lines** such as ZR-75-1 human breast cancer cells and CHO-K1 Chinese hamster ovary cells.

ST spermine analog prepn **polyamine transport inhibitor**; anticancer agent spermine analog prepn

IT Amines, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (**polyamines**, nonpolymeric; prepn. of spermine analogs for use as **polyamine transport inhibitors**)

IT Antitumor agents  
 Biological transport  
 (prepn. of spermine analogs for use as **polyamine**

PAGE 1-A


$$\begin{array}{c} \text{NH}-(\text{CH}_2)_3-\text{NH}_2 \\ | \\ -\text{CH}-(\text{CH}_2)_3-\text{NH}-(\text{CH}_2)_3-\text{NH}_2 \end{array}$$

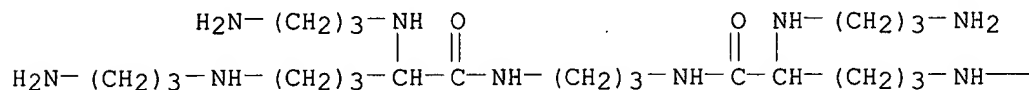
IT 206760-67-0P 206760-68-1P 206760-69-2P  
206760-70-5P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

RN 206760-67-0 HCAPLUS

CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



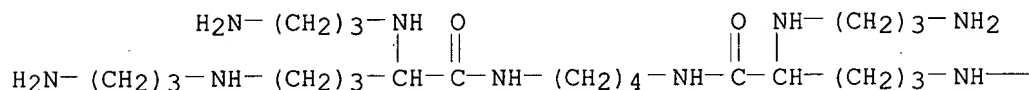
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-68-1 HCAPLUS

CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



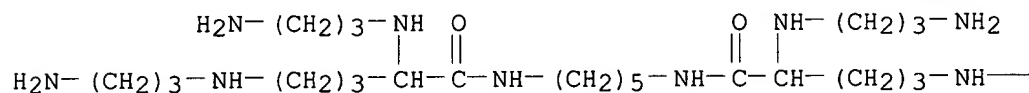
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-69-2 HCAPLUS

CN Pentanamide, N,N'-1,5-pentanediyilbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



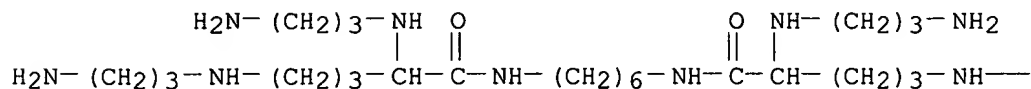
PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

RN 206760-70-5 HCAPLUS

CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

L119 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:269701 HCAPLUS

DN 126:340122

TI Transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers

AU Sakai, Naomi; Matile, Stefan

CS Department of Chemistry, Georgetown University, Washington, DC, 20057-1227, USA

SO Tetrahedron Letters (1997), 38(15), 2613-2616

CODEN: TELEAY; ISSN: 0040-4039

PB Elsevier

DT Journal

LA English

CC 6-1 (General Biochemistry)

OS CASREACT 126:340122

AB A series of amphiphilic **polyamine** dendrimers was efficiently prepd. from cholestamine to probe the hypothesis that an increasing no. of ammonium cations attached to a hydrophobic anchoring group should increasingly facilitate transmembrane ion **transport**. Results from **transport** expts. using large unilamellar vesicles are consistent with this new concept.

ST **transport** membrane bilayer **polyamine** amphiphilic

IT Membrane, biological

(bilayer; transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT Amines, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(**polyamines**, nonpolymeric; transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT **Biological transport**

(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT 189879-66-1 189879-67-2 189879-68-3

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT 2206-20-4P 189879-70-7P 189879-73-0P 189879-79-6P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or

reagent)

(transmembrane ion **transport** mediated by amphiphilic  
**polyamine** dendrimers)

IT 189879-77-4P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP  
(Properties); SPN (Synthetic preparation); **BIOL (Biological study)**  
; PREP (Preparation); PROC (Process)

(transmembrane ion **transport** mediated by amphiphilic  
**polyamine** dendrimers)

IT 189879-77-4P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP  
(Properties); SPN (Synthetic preparation); **BIOL (Biological study)**  
; PREP (Preparation); PROC (Process)

(transmembrane ion **transport** mediated by amphiphilic  
**polyamine** dendrimers)

RN 189879-77-4 HCAPLUS

CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-  
aminopropyl)amino]propyl]-N'-[3-[[3-(3.alpha.,5.alpha.)-cholestan-3-  
yl]amino]propyl]-, octakis(trifluoroacetate) (9CI) (CA INDEX NAME)

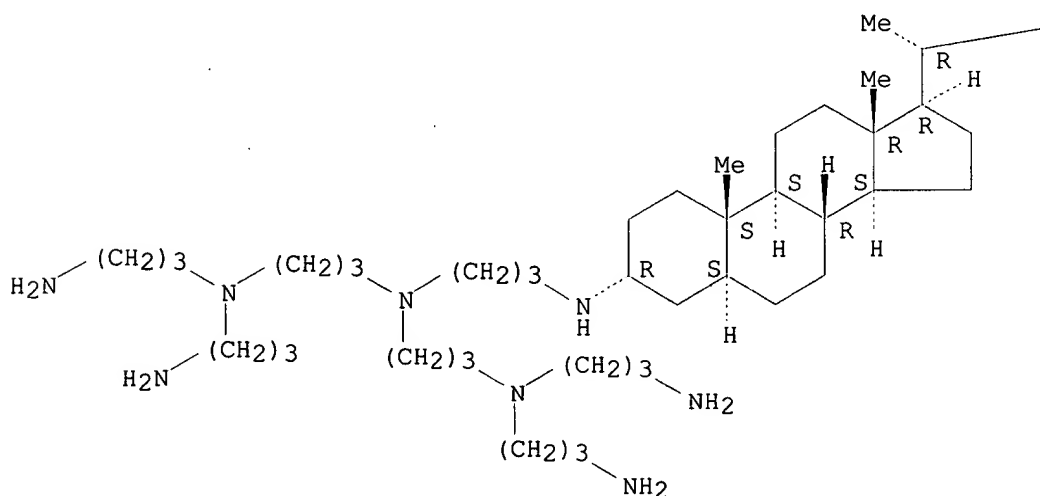
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CRN 189879-76-3

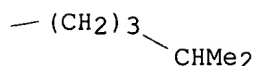
CMF C48 H98 N8

Absolute stereochemistry.

PAGE 1-A



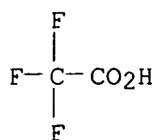
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L119 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:681591 HCAPLUS

DN 126:42328

TI 2,2'-Dithiobis(N-ethyl-spermine-5-carboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system

AU Huber, Maria; Pelletier, Joele G.; Torossian, Krikor; Dionne, Patricia; Gamache, Isabelle; **Charest-Gaudreault, Rene; Audette, Marie; Poulin, Richard**

CS Laboratory Molecular Endocrinology, Laval University Medical Research Center, Ste. Foy, QC, G1V 4G2, Can.

SO Journal of Biological Chemistry (1996), 271(44), 27556-27563  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 1-6 (Pharmacology)

AB We have synthesized 2,2'-dithiobis(N-ethyl-spermine-5-carboxamide) (DESC), its thiol monomer (MESC), and the mixed MESC-cysteamine disulfide (DEASC) as potential **inhibitors of polyamine transport** in mammalian cells. DESC was the most potent antagonist of spermine **transport** in ZR-75-1 human breast cancer cells, with  $K_i$  values of  $5.0 \pm 0.7$ ,  $80 \pm 31$ , and  $16 \pm 3$   $\mu\text{M}$  for DESC, MESC, and DEASC, resp. DESC also strongly blocked putrescine and spermidine uptake in ZR-75-1 cells ( $K_i = 1.6 \pm 0.5$  and  $2.7 \pm 1.1$   $\mu\text{M}$ , resp.). While DESC and MESC were purely competitive **inhibitors of putrescine transport**, DEASC was a mixed competitive/noncompetitive antagonist. Remarkably, DESC was virtually impermeant in ZR-75-1 cells despite its low  $K_i$  toward **polyamine transport**. The marked difference in affinity between DESC and MESC was essentially due to the tail-to-tail juxtaposition of two spermine-like structures, suggesting that dimeric ligands of the **polyamine transporter** might simultaneously interact with more than one binding site. While DESC strongly decreased the initial rate of  $[^3\text{H}]$ spermidine **transport**, even a 40-fold molar excess of antagonist could not completely abolish intracellular spermidine accumulation. Moreover, as little as  $0.3$   $\mu\text{M}$  spermidine fully restored growth in ZR-75-1 cells treated with an **inhibitor of polyamine biosynthesis** in the presence of  $50$   $\mu\text{M}$  DESC, thus emphasizing the importance of uptake of trace amts. of exogenous **polyamines**. Thus, reducing the exogenous supply of **polyamines** with a potent competitive **inhibitor** may be kinetically inadequate to block replenishment of the **polyamine pool in polyamine-depleted tumor cells that display high transport capacity**. These results demonstrate that **polyamine** analogs cross-linked into a dimeric structure such as DESC interact with high affinity with the mammalian **polyamine carrier** without being used as substrates. These novel properties provide a framework for the design of specific irreversible **inhibitors of the polyamine transporter**, which should present advantages over competitive antagonists for an efficient blockade of **polyamine transport in tumor cells**.

ST antitumor dithiobisethylsperminecarboxamide deriv membrane **polyamine transport**

IT Antitumor agents.

**Biological transport**

Cell membrane

Neoplasm

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT Antitumor agents

(mammary gland; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT Mammary gland

(neoplasm, **inhibitors**; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT Amines, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**polyamines**, nonpolymeric; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 184895-97-4P 184895-98-5P 184895-99-6P 184896-00-2P  
184896-01-3P 184896-02-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 71-44-3, Spermine 110-60-1, Putrescine 124-20-9, Spermidine

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 51-85-4, Cystamine 56-17-7, Cystamine dihydrochloride 6211-16-1, Ornithine dihydrochloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 124076-28-4P 184896-03-5P 184896-04-6P 184896-05-7P 184896-06-8P  
184896-07-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 184896-08-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

IT 184895-97-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport system**)

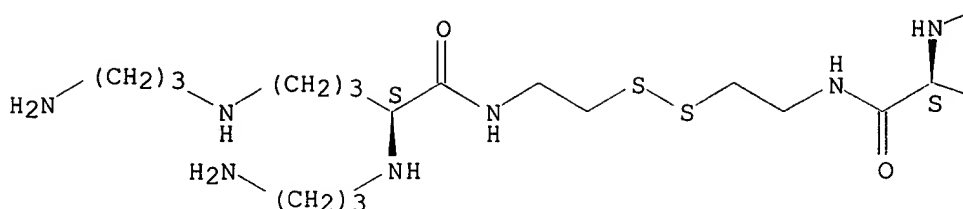
RN 184895-97-4 HCAPLUS

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)-(9CI) (CA INDEX NAME)

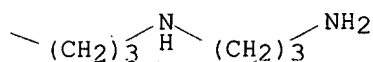
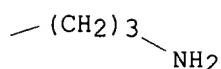


Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L119 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:456098 HCAPLUS

DN 125:107063

TI Cationic amphiphiles and plasmids for intracellular delivery of therapeutic molecules

IN Siegel, Craig S.; Harris, David J.; Lee, Edward R.; Hubbard, Shirley C.; Cheng, Seng H.; Eastman, Simon J.; Marshall, John; Scheule, Ronald K.; Yew, Nelson S.; et al.

PA Genzyme Corporation, USA

SO PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 63

FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9618372	A2	19960620	WO 1995-US16174	19951208	<--
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5650096	A	19970722	US 1994-352479	19941209	<--
	US 5747471	A	19980505	US 1995-540867	19951011	<--
	US 6071890	A	20000606	US 1995-545473	19951019	<--
	AU 9645161	A1	19960703	AU 1996-45161	19951208	<--
	AU 716706	B2	20000302			
	EP 799059	A1	19971008	EP 1995-943769	19951208	<--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 10510813	T2	19981020	JP 1995-519236	19951208	<--
	AU 9732315	A1	19980417	AU 1997-32315	19970610	<--
	AU 736143	B2	20010726			
	EP 1007003	A1	20000614	EP 1997-927989	19970610	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

	JP 2001500897	T2	20010123	JP 1998-515603	19970610 <--
	US 2002013282	A1	20020131	US 1998-166074	19981005 <--
PRAI	US 1994-352479	A	19941209	<--	
	US 1995-4344P	P	19950926	<--	
	US 1995-4399P	P	19950927	<--	
	US 1995-540867	A	19951011	<--	
	US 1995-545473	A	19951019	<--	
	WO 1995-US16174	W	19951208	<--	
	WO 1997-US9748	W	19970610	<--	
OS	MARPAT 125:107063				
AB	<p>Novel cationic amphiphiles are provided that facilitate <b>transport</b> of biol. active (therapeutic) mols. into cells. The amphiphiles contain lipophilic groups derived from steroids, from mono or dialkylamines, or from alkyl or acyl groups; and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines or polyalkylamines. Thus, N4-spermidine cholesteryl carbamate provided an .apprx.20-fold enhancement of the transfection ability of plasmid pCMVHI-CAT (chloramphenicol acetyltransferase-encoding) in mice. There are provided also therapeutic comps. prepd. typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols. Therapeutic mols. that can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic comps. of the invention include providing gene therapy, and delivery of antisense polynucleotides of biol. active polypeptides to cells. With respect to therapeutic comps. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation. Several vectors were constructed for improved delivery of the gene the cystic fibrosis transmembrane conductance regulator (CFTR) under control of the human cytomegalovirus promoter/enhancer during cationic amphiphile-mediated gene transfer. Addnl., targeting of organs for gene therapy by i.v. administration of therapeutic comps. is described. Syntheses are described for N4-spermine cholesteryl carbamate, N4-(N'-cholesteryl carbamate glycineamide)-spermine, N4-spermidine-2,3-dilauryloxypropylamine, and N4-spermine-2,3-dilauryloxypropylamine.</p>				
ST	cationic amphiphile transfection plasmid gene therapy; inflammation cytokine gene therapy plasmid transfection; cystic fibrosis CFTR gene therapy plasmid				
IT	Cystic fibrosis				
	Inflammation				
	Inflammation inhibitors				
	Pharmaceuticals				
	Transformation, genetic				
	(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)				
IT	Lymphokines and Cytokines				
	Ribozymes				
	RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)				
	(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)				
IT	Gene				
	Ribonucleic acids, messenger				
	RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)				
	(encoding therapeutic protein; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)				
IT	Plasmid and Episome				
	(pCF1; cationic amphiphiles and plasmids for intracellular delivery of				

- therapeutic mols.)
- IT Plasmid and Episome  
(pCMV-CFTR; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Plasmid and Episome  
(pMyc4-CFTR; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Glycophosphoproteins  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(CFTR (cystic fibrosis transmembrane conductance regulator), cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Gene, animal  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DHFR, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Ribonucleic acids  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(antisense, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Gene, animal  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(c-myc, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Amphiphiles  
(cationic, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Deoxyribonucleic acids  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(complementary, encoding therapeutic protein; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Deoxyribonucleic acids  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(complementary, antisense, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Genetic element  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(enhancer element, from human cytomegalovirus, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Therapeutics  
(geno-, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(interleukin 1, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(interleukin 1 receptor antagonist, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

- (interleukin 11, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(interleukin 2, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(interleukin 6, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(interleukin 8, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Lymphokines and Cytokines  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(monocyte chemoattractant protein 1, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Genetic element  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ori, from human .beta.-globin gene, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Plasmid and Episome  
(pCF2, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Genetic element  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyadenylation signal, from bovine growth hormone, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Genetic element  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(promoter, from human cytomegalovirus, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Genetic element  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transposon Tn903, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT Phosphoproteins  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(tumor suppressor, p53, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 9041-92-3, .alpha.1-Antitrypsin 83869-56-1, Granulocyte-macrophage colony-stimulating factor 123626-67-5, Endothelin-1 124861-55-8, Proteinase inhibitor, TIMP-2 140208-24-8, Proteinase inhibitor, TIMP-1  
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-63-9P  
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 80-97-7, Dihydrocholesterol 85-41-6, Phthalimide 100-46-9, Benzylamine, reactions 107-13-1, 2-Propenenitrile, reactions 112-99-2 628-20-6, 4-Chlorobutyronitrile 910-31-6, Cholesteryl chloride 4799-67-1, 3-Benzoyloxy-1,2-propanediol 14611-34-8 30189-36-7 51323-71-8, Dodecylmethanesulfonate 179075-72-0  
RL: RCT (Reactant)  
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P 179075-61-7P 179075-62-8P 179075-64-0P 179075-65-1P 179075-66-2P 179075-67-3P 179075-68-4P 179075-69-5P 179075-70-8P 179075-71-9P 179075-73-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 2462-63-7  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-lipid for transfection; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 57-50-1, biological studies 59-23-4, Galactose, biological studies 63-42-3 69-65-8, Mannitol 69-79-4 99-20-7, Trehalose  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(excipient; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 3392-07-2  
RL: RCT (Reactant)  
(synthesis of (cholesteryl carbamate glycineamide)spermine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-54-8P 179075-55-9P 179075-56-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of (cholesteryl carbamate glycineamide)spermine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 20255-94-1 89965-56-0 179075-58-2  
RL: RCT (Reactant)  
(synthesis of spermidine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-57-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of spermidine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 71-44-3, Spermine 7144-08-3, Cholesteryl chloroformate  
RL: RCT (Reactant)  
(synthesis of spermine cholesteryl carbamate; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-52-6P 179075-53-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of spermine cholesteryl carbamate; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-59-3  
RL: RCT (Reactant)  
(synthesis of spermine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179075-60-6  
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transfection-enhancing agent; anionic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
- IT 179074-99-8 179075-00-4 179075-01-5 179075-02-6 179075-03-7 179075-04-8 179075-05-9 179075-06-0 179075-07-1 179075-08-2 179075-09-3 179075-10-6 179075-11-7 179075-12-8

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179075-43-5	179075-44-6	179075-45-7	179075-46-8	179075-47-9
179075-48-0	179075-49-1	179075-50-4	179075-51-5	179075-74-2

RL: BAC (Biological activity or effector, except adverse);

THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(transfection-enhancing agent; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-09-3

RL: BAC (Biological activity or effector, except adverse);

THU (Therapeutic use); BIOL (Biological study);

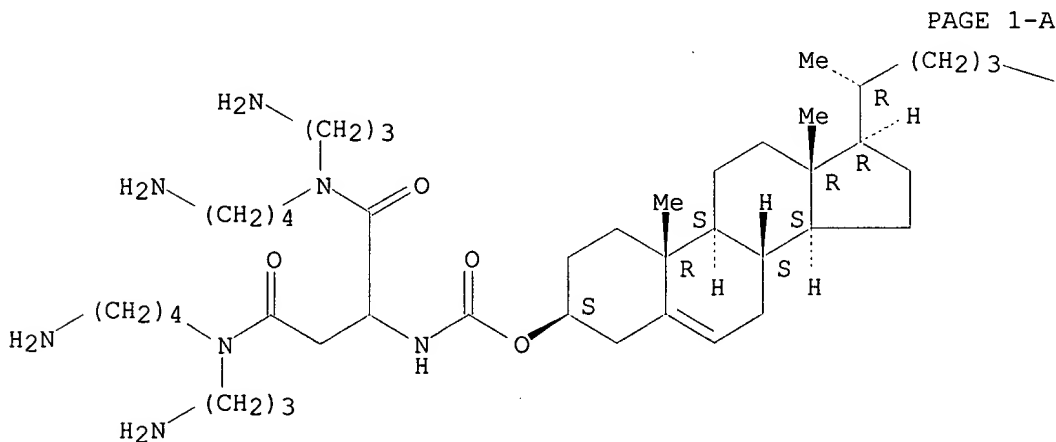
USES (Uses)

(transfection-enhancing agent; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

RN 179075-09-3 HCAPLUS

CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[ (4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe2

L119 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:463054 HCAPLUS

DN 119:63054

TI Calcium receptor-active molecules

IN Nemeth, Edward F.; Van Wagenen, Bradford C.; Balandrin, Manuel F.

PA NPS Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-566

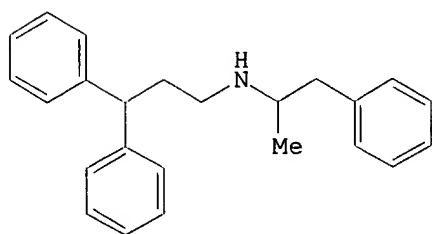
ICS G01N033-567; C07C211-02; C07C211-16; C07C211-27; C07H021-00;  
C07K005-00; C07K007-00; C12N015-12; A61K037-02

CC 1-10 (Pharmacology)

Section cross-reference(s): 9, 63

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9304373	A1	19930304	WO 1992-US7175	19920821	<--
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG					
	AU 9225889	A1	19930316	AU 1992-25889	19920821	<--
	AU 673500	B2	19961114			
	JP 06510531	T2	19941124	JP 1992-504650	19920821	<--
	JP 2728564	B2	19980318			
	EP 657029	A1	19950614	EP 1992-919933	19920821	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
	JP 09281209	A2	19971031	JP 1996-232165	19920821	<--
	JP 09328420	A2	19971222	JP 1996-232130	19920821	<--
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	JP 3256502	B2	20020212			
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	JP 2001220356	A2	20010814	JP 2000-394979	19920821	<--
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	CN 1067550	B	20010627			
	IL 102917	A1	20001206	IL 1992-102917	19920823	<--
	ZA 9206360	A	19930330	ZA 1992-6360	19920824	<--
	NO 9400581	A	19940425	NO 1994-581	19940221	<--
	AU 9671977	A1	19970220	AU 1996-71977	19961125	<--
	AU 711247	B2	19991007			
	AU 9931226	A1	19990722	AU 1999-31226	19990524	<--
PRAI	US 1991-749451	A2	19910823			<--
	US 1992-834044	A2	19920211			<--
	US 1992-934161	A2	19920821			<--
	JP 1992-504650	A3	19920821			<--
	JP 1996-232165	A3	19920821			<--
	JP 1998-313631	A3	19920821			<--
	WO 1992-US7175	A	19920821			<--
	US 1993-141248	A	19931022			<--
	US 1994-292827	A	19940819			<--
	AU 1994-80872	A3	19941021			<--
OS	MARPAT 119:63054					
GI						



I

AB Methods, compns., and compds. are disclosed for treating a patient having a disease characterized by an abnormal level of component(s), the activity of which is regulated or affected by the activity of .gtoreq.1 Ca<sup>2+</sup> receptors. The compds. act as agonists or antagonists of the Ca<sup>2+</sup>

receptors, preferably selective to receptors on parathyroid cells, bone osteoclasts, juxtaglomerular kidney cells, proximal tubule kidney cells, keratinocytes, parafollicular thyroid cells, and placental trophoblasts. A method for diagnosis of a disease comprises identifying the no. and/or location of  $\text{Ca}^{2+}$  receptors and making a comparison to that of normal subjects. Methods for identifying useful therapeutic mols. are also disclosed. Structure-function (intracellular  $\text{Ca}^{2+}$ -mobilizing) studies were done on aminoglycosides and other compds. on various cells. Recombinant  $\text{Ca}^{2+}$  receptor protein mRNAs were expressed in *Xenopus* oocytes. Compd. NPS 449 (I) caused a concn.-dependent inhibition of bone resorption with an  $\text{IC}_{50}$  of 10  $\mu\text{M}$ .

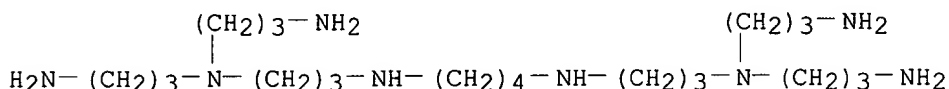
- ST calcium receptor agonist antagonist
- IT Blood
  - Blood serum
    - (calcium of, redn. of, by calcium receptor-active NPS 467)
- IT Osteoclast
  - (calcium receptor on)
- IT Trophoblast
  - (calcium receptor on, of placenta)
- IT Antihypertensives
  - (calcium receptor-active mols.)
- IT Pharmaceutical analysis
  - (calcium receptor-active mols. identification in, screening method for)
- IT Immunoassay
  - (calcium receptors detn. by, for disease diagnosis)
- IT Neoplasm
  - (diagnosis of, calcium receptors detn. in)
- IT Gene, animal
  - RL: BIOL (Biological study)
  - (for calcium receptor)
- IT Ribonucleic acids, messenger
  - RL: BIOL (Biological study)
  - (for exogenous calcium receptor, chloride ion conductance increase in *Xenopus* oocyte elicitation by)
- IT Neoplasm inhibitors
  - (for hypercalcemia-causing tumors, calcium receptor-active mols.)
- IT Protamines
  - RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
  - (intracellular calcium-mobilizing activity of)
- IT Diagnosis
  - (of calcium-related diseases or conditions, calcium receptors detn. in)
- IT *Xenopus*
  - Xenopus laevis*
    - (oocytes of, chloride ion conductance increase in, exogenous calcium receptor mRNA elicitation of)
- IT Parathyroid gland
  - (parathyroid hormone secretion by cells of, intracellular calcium levels-affecting substance inhibition of)
- IT Peptides, biological studies
  - RL: BIOL (Biological study)
  - (pos.-charged, calcium receptor-active mols.)
- IT Bone, metabolism
  - (resorption of, intracellular calcium levels-affecting substance inhibition of)
- IT Antibodies
  - RL: BIOL (Biological study)
  - (to calcium receptors, for immunoassay for disease diagnosis)
- IT Osteoporosis
  - (treatment of, with calcium receptor-active mols.)
- IT Placenta
  - (trophoblasts of, calcium receptor on)
- IT Thyroid gland, composition



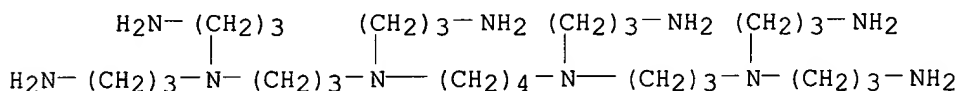
- (C cell, calcium receptor on)
- IT Bone, disease
  - (Paget's, treatment of, with calcium receptor-active mols.)
- IT Amines, biological studies
  - RL: BIOL (Biological study)
  - (alkaryl, calcium receptor-active mols.)
- IT Glycosides
  - RL: BAC (Biological activity or effector, except adverse); BIOL
  - (Biological study)
  - (amino, intracellular calcium-mobilizing activity of)
- IT **Polyamines**
  - RL: BIOL (Biological study)
  - (branched, calcium receptor-active mols.)
- IT Ion channel blockers
  - Ion channel openers
  - (calcium, pharmaceuticals)
- IT Receptors
  - RL: BIOL (Biological study)
  - (calcium, substances binding and active with, of osteoclasts and other cells)
- IT Molecular structure-biological activity relationship
  - (calcium-mobilizing, intracellular, of aminoglycosides and other polyamines)
- IT Glycerides, biological studies
  - RL: BIOL (Biological study)
  - (di-, intracellular calcium levels-affecting substance causing increase in)
- IT Kidney, composition
  - (juxtaglomerular cell, calcium receptor on)
- IT Skin, composition
  - (keratinocyte, calcium receptor on)
- IT Parathyroid gland
  - (neoplasm, diagnosis of, calcium receptors detn. in)
- IT Egg
  - (oocyte, chloride ion conductance increase in, of Xenopus, exogenous calcium receptor mRNA elicitation of)
- IT Pharmaceutical dosage forms
  - (oral, of calcium receptor-active NPS 467 isomer, blood serum calcium lowering with)
- IT **Amines**, biological studies
  - RL: BIOL (Biological study)
  - (poly-, cyclic, calcium receptor-active mols.)
- IT Hyperparathyroidism
  - (primary, treatment of, with calcium receptor-active mols.)
- IT Kidney, composition
  - (proximal tubule, calcium receptor on cell of)
- IT Hyperparathyroidism
  - (secondary, treatment of, with calcium receptor-active mols.)
- IT **Biological transport**
  - (translocation, of intracellular calcium, calcium receptor-active substances effect on)
- IT 51-61-6, Dopamine, biological studies 7683-59-2, Isoproterenol
  - RL: BIOL (Biological study)
  - (cAMP formation stimulated by, intracellular calcium levels-affecting substance inhibition of)
- IT 148740-51-6
  - RL: BAC (Biological activity or effector, except adverse); BIOL
  - (Biological study)
  - (calcilytic activity of, on parathyroid cells)
- IT 390-64-7 13042-18-7 108448-58-4 114753-78-5 133805-32-0 148717-48-0 148717-50-4
  - RL: BIOL (Biological study)
  - (calcium receptor-active mol.)

- IT 108393-62-0D, derivs.  
RL: BIOL (Biological study)  
(calcium receptor-active mols.)
- IT 16887-00-6, Chloride ion, biological studies  
RL: PRP (Properties)  
(conductance of, increase in, in Xenopus oocytes injected with mRNA for calcium receptor)
- IT 60-92-4, CAMP  
RL: FORM (Formation, nonpreparative)  
(formation of, dopamine- or isoproterenol-stimulated, intracellular calcium levels-affecting substance inhibition of)
- IT 16561-29-8, Phorbol myristate acetate 34807-41-5, Mezerein 90365-57-4, (-)-Indolactam V  
RL: BIOL (Biological study)  
(intracellular calcium levels-affecting substance activity inhibition by)
- IT 141436-78-4, Protein kinase C  
RL: BIOL (Biological study)  
(intracellular calcium levels-affecting substance activity inhibition by activator of)
- IT 88269-39-0, Inositol-1,4,5-triphosphate  
RL: BIOL (Biological study)  
(intracellular calcium levels-affecting substance causing increase in)
- IT 7681-49-4, Sodium fluoride, biological studies  
RL: BIOL (Biological study)  
(intracellular calcium levels-affecting substance inhibition by)
- IT 7439-96-5, Manganese, biological studies  
RL: BIOL (Biological study)  
(intracellular calcium-mobilizing activity of)
- IT 52-53-9 57-92-1, Streptomycin, biological studies 71-44-3, Spermine 112-24-3, Triethylenetetramine 112-57-2, Tetraethylenepentamine 119-04-0, Neomycin B 124-20-9, Spermidine 154-21-2, Lincomycin 296-35-5, Hexacyclen 1403-66-3, Gentamicin 2783-17-7, 1,12-Diaminododecane 4067-16-7, Pentaethylenehexamine 4696-76-8, Bekanamycin 8063-07-8, Kanamycin 16662-47-8 24937-47-1 25104-18-1 25212-18-4 38000-06-5 42399-41-7, Diltiazem 57818-92-5, TMB-8 87955-89-3 105029-41-2, Argiotoxin 636 111944-83-3, Argiotoxin 659 115976-91-5, Philanthotoxin 433 128549-96-2, Agatoxin 489 128549-97-3 139750-76-8, Budmunchiamine A 148717-51-5 148717-52-6 148717-53-7 148740-50-5  
RL: BAC (Biological activity or effector, except adverse);  
BIOL (Biological study)  
(intracellular calcium-mobilizing activity of)
- IT 159149-75-4P  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of and bovine parathyroid cell calcium receptor activation by)
- IT 148717-54-8P 148717-55-9P 148717-56-0P 148740-52-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of and bovine parathyroid cell calcium receptor activation by)
- IT 148717-47-9P 148717-49-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of and calcium receptor activity of)
- IT 13042-18-7DP, Fendiline, analogs 13042-18-7P, Fendiline  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, calcium receptor-active substances in relation to)
- IT 5586-73-2  
RL: RCT (Reactant)  
(reaction of, with acetophenone, in prepn. of calcium receptor-active substance)
- IT 98-86-2, Acetophenone, reactions  
RL: RCT (Reactant)  
(reaction of, with bisphenylpropylamine, in prepn. of calcium

receptor-active substance)  
 IT 2038-57-5, 3-Phenylpropylamine 18655-48-6  
 RL: RCT (Reactant)  
 (reaction of, with methoxyacetophenone)  
 IT 586-37-8, 3'-Methoxyacetophenone  
 RL: RCT (Reactant)  
 (reaction of, with phenylpropylamine)  
 IT 9002-64-6, Parathyroid hormone  
 RL: BIOL (Biological study)  
 (secretion of, by parathyroid cell, intracellular calcium  
 levels-affecting substance inhibition of)  
 IT 9007-12-9, Calcitonin  
 RL: BIOL (Biological study)  
 (secretion of, stimulation of, with calcium receptor-binding substance)  
 IT 7440-70-2, Calcium, biological studies  
 RL: BIOL (Biological study)  
 (substances increasing or blocking intracellular)  
 IT 148717-51-5 148740-50-5  
 RL: BAC (Biological activity or effector, except adverse);  
 BIOL (Biological study)  
 (intracellular calcium-mobilizing activity of)  
 RN 148717-51-5 HCAPLUS  
 CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,17-bis(3-aminopropyl)- (9CI)  
 (CA INDEX NAME)



RN 148740-50-5 HCAPLUS  
 CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,8,13,17-tetrakis(3-aminopropyl)-  
 (9CI) (CA INDEX NAME)



L119 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1992:105949 HCAPLUS

DN 116:105949

TI .alpha.-Methyl **polyamines**: metabolically stable spermidine and  
 spermine mimics capable of supporting growth in cells depleted of  
**polyamines**

AU Lakanen, John R.; Coward, James K.; Pegg, Anthony E.

CS Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA

SO J. Med. Chem. (1992), 35(4), 724-34

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

CC 26-9 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 6

AB In order to assess the tolerance of the target enzyme spermine synthase  
 for .alpha.-substituents on the aminopropyl moiety of the substrate  
 spermidine, 1-methylspermidine (I) was synthesized. I is a poor substrate  
 for spermine synthase and is not a substrate for spermidine  
 N1-acetyltransferase, suggesting that .alpha.-methylated  
**polyamines** might be metabolically stable and therefore useful  
 tools for studying **polyamine** effects in intact cells. On the

basis of initial cellular results with I, 1-methylspermine (II) and 1,12-dimethylspermine (III) were also synthesized. When added to cells (L1210, SV-3T3, or HT29) depleted of both putrescine and spermidine by prior treatment with .alpha.-(difluoromethyl)ornithine (IV), these .alpha.-methylated **polyamines** were able to restore cell growth to that obsd. in the absence of IV. In accord with the enzyme data noted above, metabolic studies indicated a slow conversion of I to II, but no metab. of III in these cells. It was concluded from these results that the .alpha.-methylated **polyamines** are able to substitute for the natural **polyamines**, spermidine and spermine in crit. biochem. processes which involve **polyamines** for continued cell growth. In accord with the hypothesis, preliminary data indicate that I and III are as effective as spermidine and spermine, resp., in promoting the conversion of B-DNA to Z-DNA.

ST methylspermidine prepn enzyme substrate; methylspermine prepn enzyme substrate; spermine synthase substrate methylspermidine; spermidine acetyltransferase substrate methylspermidine; **polyamine** transport system methylspermidine

IT **Biological transport**

(of **polyamines**, methylspermines and methylspermidines in study of)

IT 64885-84-3, Spermidine-N1-acetyltransferase

RL: RCT (Reactant)

(methylspermidines and methylspermines as substrates for)

IT 137945-95-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and deblocking of)

IT 66917-07-5P 137945-96-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and hydrazinolysis of)

IT 66917-06-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and hydrogenation of)

IT 138051-81-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with aminobutylphthalimide)

IT 62146-62-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with aminobutyric acid)

IT 5394-18-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with azide)

IT 35517-18-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with azidobutyrate)

IT 18523-47-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with azidobutylbutanediamine)

IT 137964-65-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with azidopropionate)

IT 137945-97-2P 137945-98-3P 137945-99-4P 137946-00-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and redn. of)

IT 137945-92-7P 137945-93-8P **137945-94-9P**

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

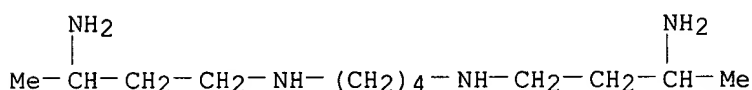
IT 137946-01-1P 137946-02-2P **137946-03-3P**

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as spermidine acetyltransferase substrate)

IT 71-44-3DP, Spermine, Me derivs. 124-20-9DP, Spermidine, Me derivs.

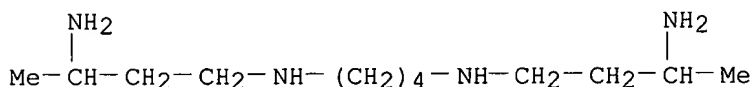
RL: PREP (Preparation) (prepn. of, as spermidine acetyltransferase substrates)

IT 110-60-1, Putrescine  
 RL: RCT (Reactant)  
 (reaction of, with aminobutyric acid)  
 IT 79-10-7, Acrylic acid, reactions 3724-65-0, Crotonic acid  
 RL: RCT (Reactant)  
 (reaction of, with azide)  
 IT 2835-82-7  
 RL: RCT (Reactant)  
 (reaction of, with butanediamine deriv.)  
 IT 137945-94-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 137945-94-9 HCAPLUS  
 CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis-, tetrahydrochloride (9CI)  
 (CA INDEX NAME)



● 4 HCl

IT 137946-03-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as spermidine acetyltransferase substrate)  
 RN 137946-03-3 HCAPLUS  
 CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis- (9CI) (CA INDEX NAME)



=> fil reg  
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TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

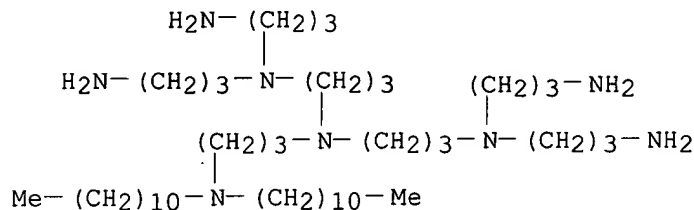
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Calculated physical property data is now available. See HELP PROPERTIES  
 for more information. See STNote 27, Searching Properties in the CAS  
 Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide can tot 1120

L120 ANSWER 1 OF 37 REGISTRY COPYRIGHT 2002 ACS  
 RN 272463-38-4 REGISTRY  
 CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(diundecylamino)propyl]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C43 H96 N8  
 SR CA  
 LC STN Files: CA, CAPLUS

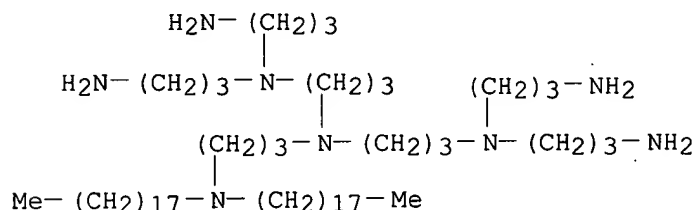


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:22412

L120 ANSWER 2 OF 37 REGISTRY COPYRIGHT 2002 ACS  
 RN 272462-73-4 REGISTRY  
 CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(dioctadecylamino)propyl]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C57 H124 N8  
 SR CA  
 LC STN Files: CA, CAPLUS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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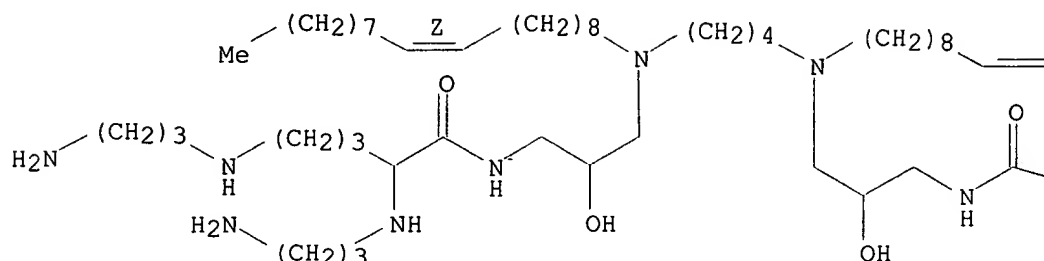
REFERENCE 1: 133:22412

L120 ANSWER 3 OF 37 REGISTRY COPYRIGHT 2002 ACS  
 RN 268554-12-7 REGISTRY  
 CN Pentanamide, N,N'-[1,4-butanediylbis[[ (9Z)-9-octadecenylimino] (2-hydroxy-3,1-propanediyl)]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

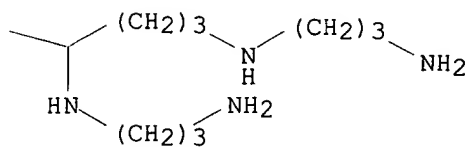
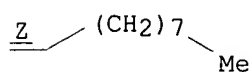
FS STEREOSEARCH  
 MF C68 H142 N12 O4  
 SR CA  
 LC STN Files: CA, CAPLUS

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 4 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN **268539-58-8** REGISTRY

CN Pentanamide, N,N'-[4,13-di-(9Z)-9-octadecenyl-7,10-dioxa-4,13-diazahexadecane-1,16-diyl]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

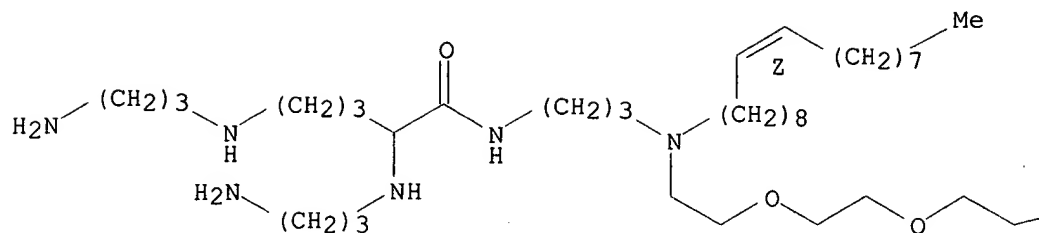
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SR CA

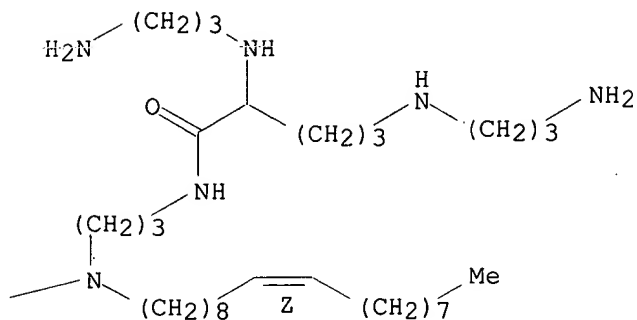
LC STN Files: CA, CAPLUS

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 5 OF 37    REGISTRY    COPYRIGHT 2002 ACS

RN 268539-54-4 REGISTRY

CN	Pentanamide, N,N'-[1,2-ethanediylbis[[ (9Z)-9-octadecenyylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]-(9CI) (CA INDEX NAME)
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FS STEREOSEARCH

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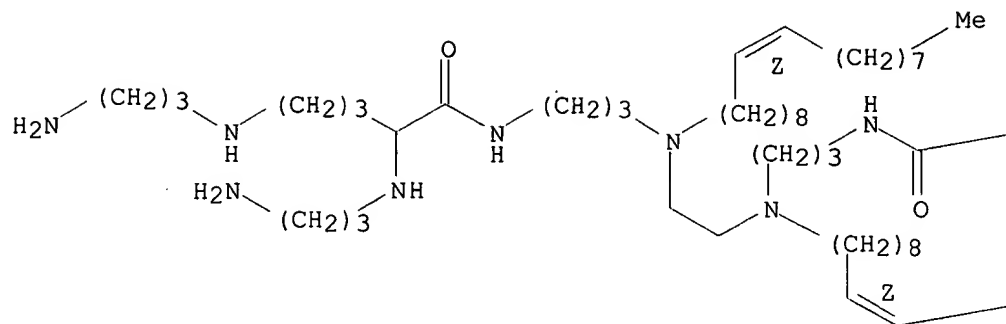
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LC STN Files: CA, CAPLUS

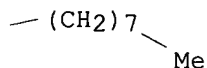
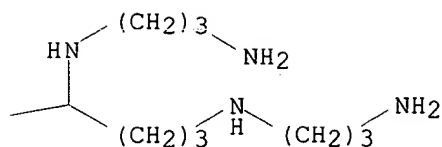
Double bond geometry as shown.



PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 6 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 268539-53-3 REGISTRY

CN Pentanamide, N,N'-[1,4-butanediylbis[[ (9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

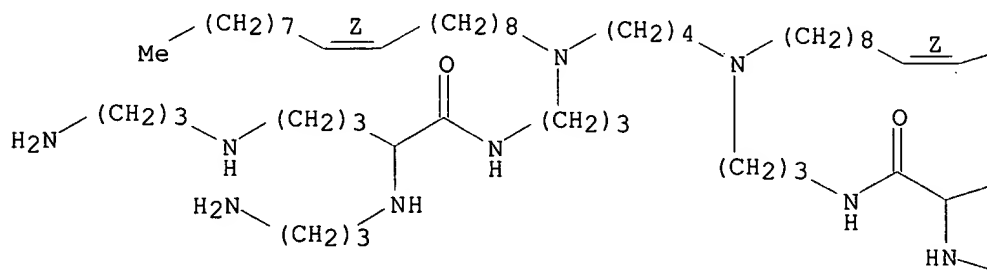
MF C68 H142 N12 O2

SR CA

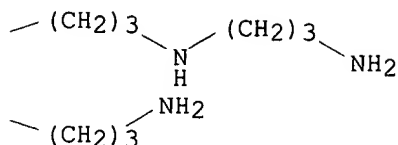
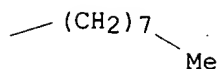
LC STN Files: CA, CAPLUS

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)  
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REFERENCE 1: 132:334312

L120 ANSWER 7 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 247187-67-3 REGISTRY

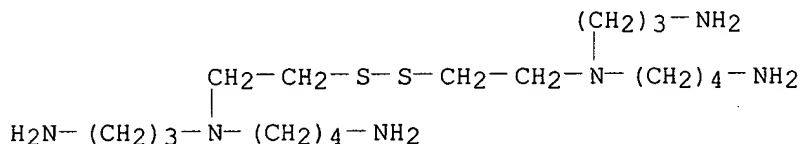
CN 1,4-Butanediamine, N,N'-(dithiodi-2,1-ethanediyl)bis[N-(3-aminopropyl)-  
(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H44 N6 S2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 131:307091

L120 ANSWER 8 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 247187-66-2 REGISTRY

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, octahydrochloride, (2S,2'S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C26 H60 N10 O2 S2 . 8 Cl H

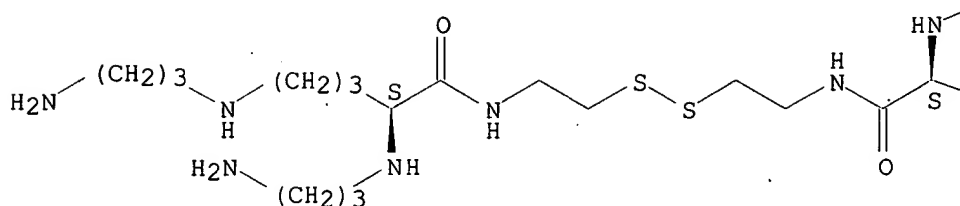
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CRN (184895-97-4)

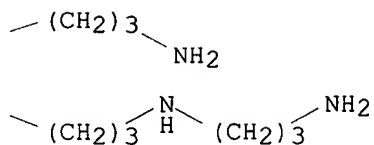
Absolute stereochemistry.

PAGE 1-A



● 8 HCl

PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

L120 ANSWER 9 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 247187-65-1 REGISTRY

CN Pentanamide, N,N'-1,5-pentanediyldis[2,5-bis[(3-aminopropyl)amino]-,  
 (2S,2'S)-(9CI) (CA INDEX NAME)

FS STEREOSEARCH

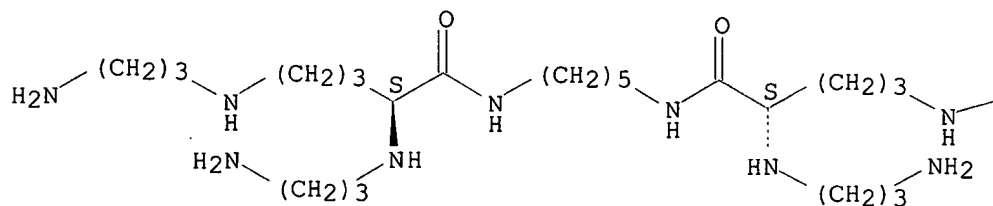
MF C27 H62 N10 O2

SR CA

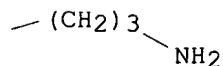
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

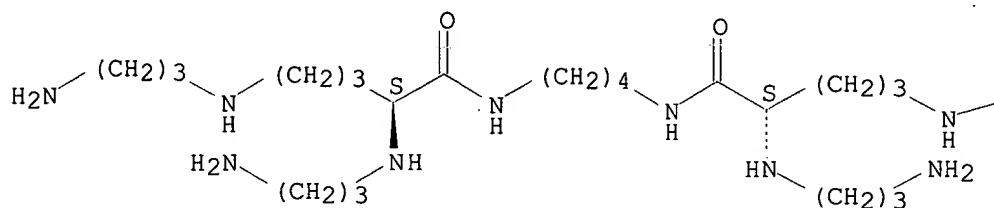
1 REFERENCES IN FILE CA (1967 TO DATE)  
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REFERENCE 1: 131:307091

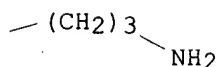
L120 ANSWER 10 OF 37 REGISTRY COPYRIGHT 2002 ACS  
RN 247187-64-0 REGISTRY  
CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]-,  
(2S,2'S)-(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C26 H60 N10 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

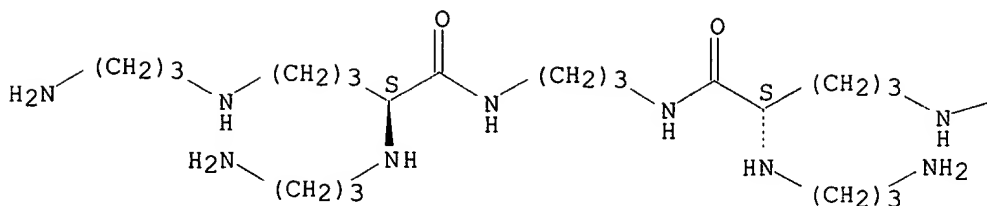
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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

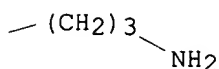
L120 ANSWER 11 OF 37 REGISTRY COPYRIGHT 2002 ACS  
RN 247187-63-9 REGISTRY  
CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]-,  
(2S,2'S)-(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C25 H58 N10 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

L120 ANSWER 12 OF 37 REGISTRY COPYRIGHT 2002 ACS

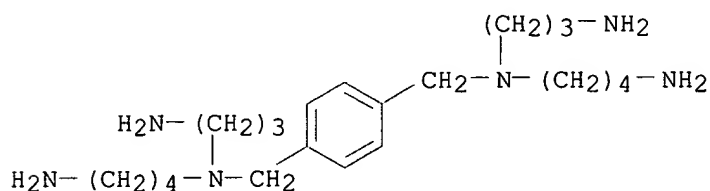
RN 244033-25-8 REGISTRY

CN 1,4-Benzenedimethanamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)

MF C22 H44 N6 . 6 Cl H

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



● 6 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 13 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 244033-24-7 REGISTRY

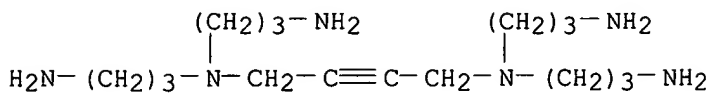
CN 2-Butyne-1,4-diamine, N,N',N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C16 H36 N6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 14 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 244033-23-6 REGISTRY

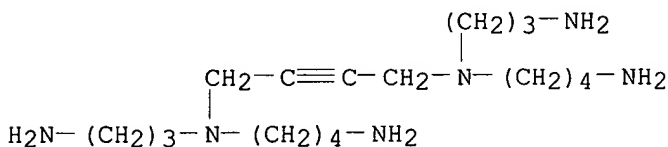
CN 2-Butyne-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-  
(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H40 N6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 15 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 244033-22-5 REGISTRY

CN 2-Butene-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)-, (2E)- (9CI) (CA  
INDEX NAME)

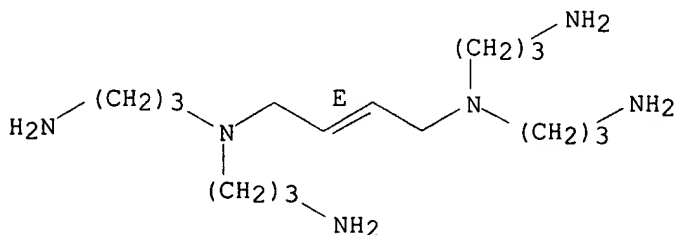
FS STEREOSEARCH

MF C16 H38 N6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Double bond geometry as shown.



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 16 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 244033-21-4 REGISTRY

CN 2-Butene-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-,  
(2E)- (9CI) (CA INDEX NAME)

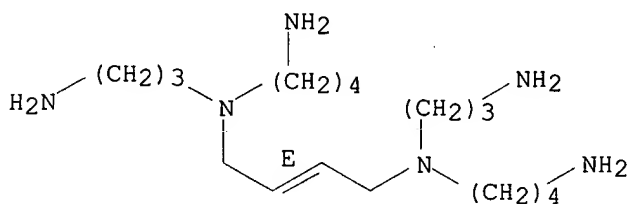
FS STEREOSEARCH

MF C18 H42 N6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Double bond geometry as shown.



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 17 OF 37 REGISTRY COPYRIGHT 2002 ACS

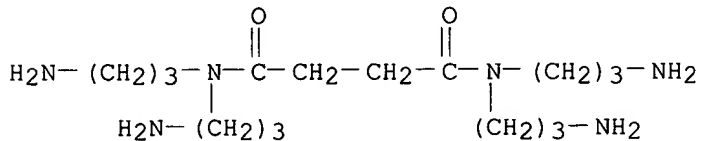
RN 244033-20-3 REGISTRY

CN Butanediamide, N,N,N',N'-tetrakis(3-aminopropyl)-, tetrahydrochloride  
(9CI) (CA INDEX NAME)

MF C16 H36 N6 O2 . 4 Cl H

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



● 4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

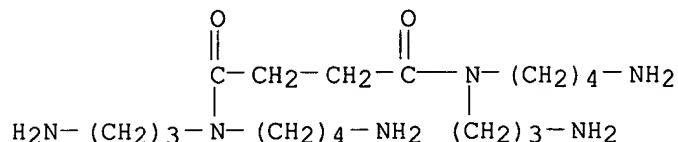
REFERENCE 1: 131:228866

L120 ANSWER 18 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 244033-19-0 REGISTRY

CN Butanediamide, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-,

tetrahydrochloride (9CI) (CA INDEX NAME)  
 MF C18 H40 N6 O2 . 4 Cl H  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

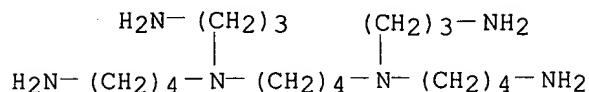


●4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 19 OF 37 REGISTRY COPYRIGHT 2002 ACS  
 RN 244033-18-9 REGISTRY  
 CN 1,4-Butanediamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)  
 MF C18 H44 N6 . 6 Cl H  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER



●6 HCl

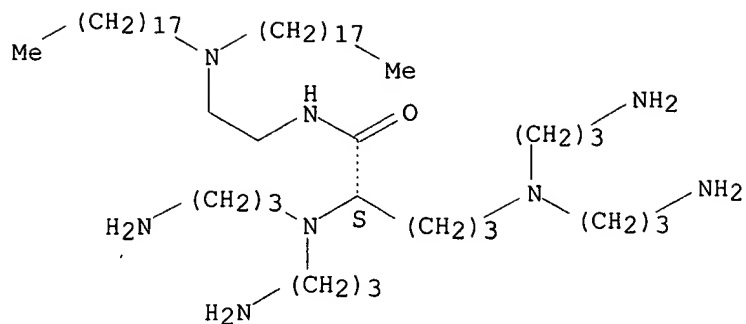
1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 20 OF 37 REGISTRY COPYRIGHT 2002 ACS  
 RN 220170-87-6 REGISTRY  
 CN Pentanamide, 2,5-bis[bis(3-aminopropyl)amino]-N-[2-(dioctadecylamino)ethyl]-, (2S)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C55 H118 N8 O  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:153974

L120 ANSWER 21 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 219304-01-5 REGISTRY

CN Glycinamide, N2,N2,N5,N5-tetrakis(3-aminopropyl)-L-ornithyl-N,N-di-octadecyl- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

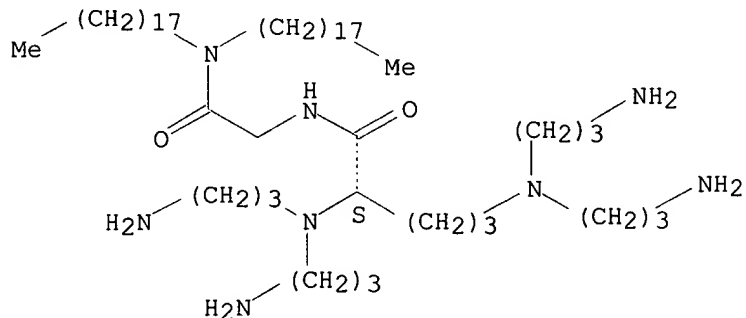
MF C55 H116 N8 O2

CI COM

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:122935

L120 ANSWER 22 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 209112-50-5 REGISTRY

CN Cholest-5-en-3-ol (3.beta.)-, [(1S)-3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)

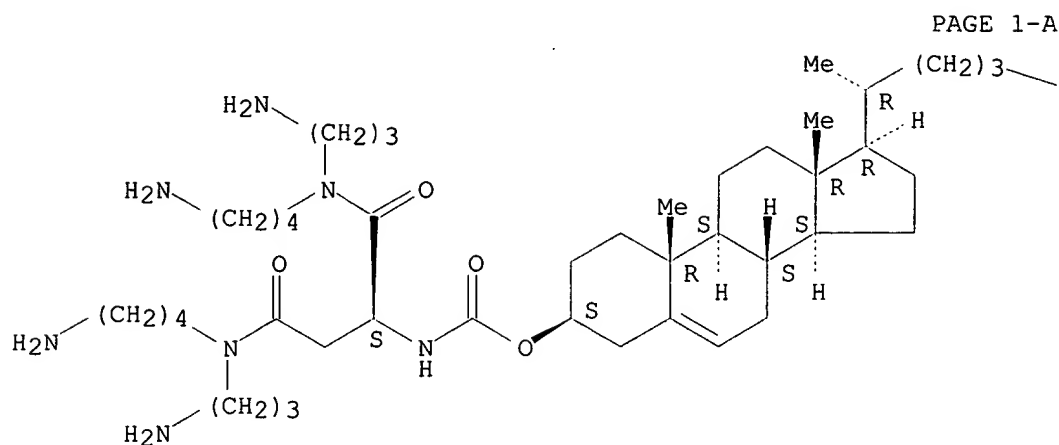
FS STEREOSEARCH

MF C46 H85 N7 O4

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PAGE 1-B

—CHMe<sub>2</sub>

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:62994

L120 ANSWER 23 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 206760-70-5 REGISTRY

CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME).

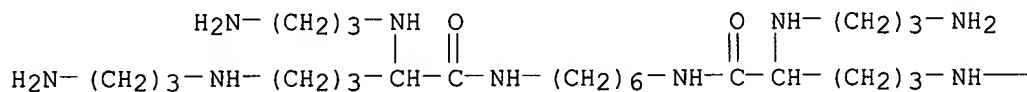
FS 3D CONCORD

MF C28 H64 N10 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

—(CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

.\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)

## 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 131:307091

REFERENCE 3: 128:321804

L120 ANSWER 24 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 206760-69-2 REGISTRY

CN Pentanamide, N,N'-1,5-pentanediyldis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

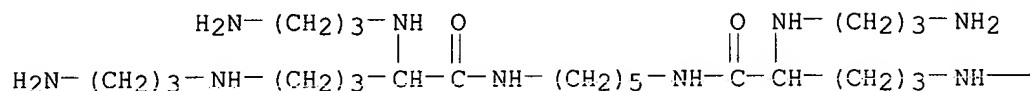
FS 3D CONCORD

MF C27 H62 N10 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 25 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 206760-68-1 REGISTRY

CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

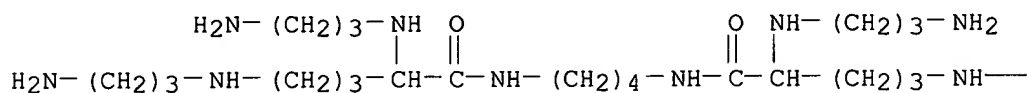
FS 3D CONCORD

MF C26 H60 N10 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 26 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 206760-67-0 REGISTRY

CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI)  
(CA INDEX NAME)

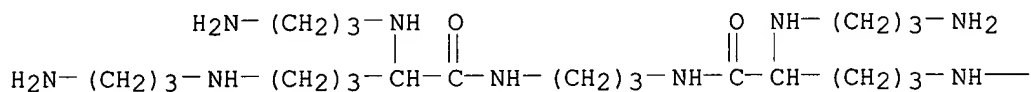
FS 3D CONCORD

MF C25 H58 N10 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH<sub>2</sub>

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 27 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 206760-63-6 REGISTRY

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

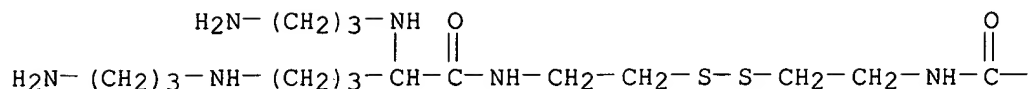
FS 3D CONCORD

MF C26 H60 N10 O2 S2

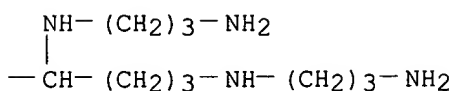
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 28 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 201859-92-9 REGISTRY

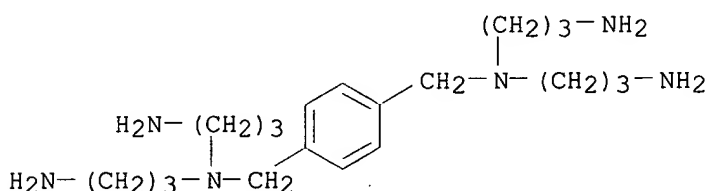
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)

MF C20 H40 N6 . 6 Cl H

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CRN (189076-31-1)



● 6 HCl

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160331

REFERENCE 2: 131:228866

REFERENCE 3: 128:135724

L120 ANSWER 29 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 189879-77-4 REGISTRY

CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-[(3.alpha.,5.alpha.)-cholestan-3-yl]amino]propyl]-, octakis(trifluoroacetate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C48 H98 N8 . 8 C2 H F3 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT

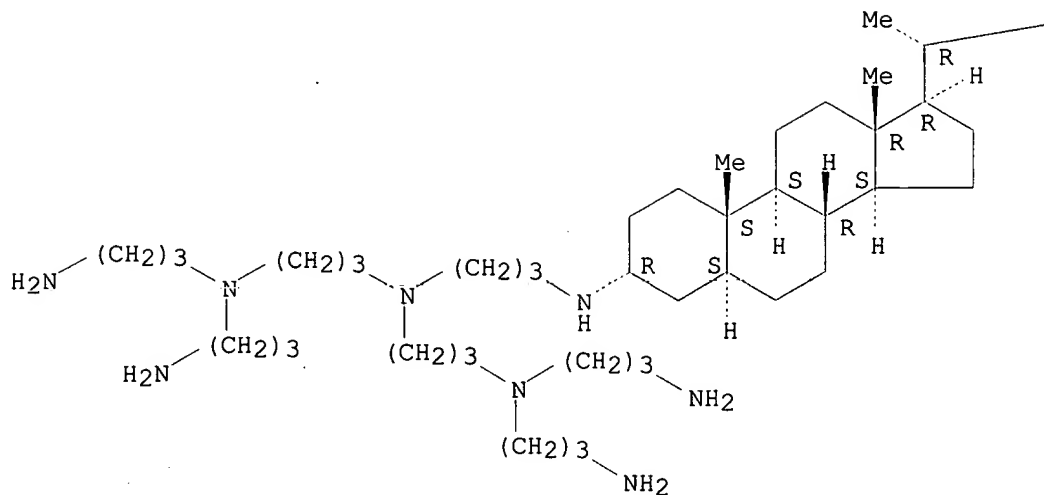
CM 1

CRN 189879-76-3

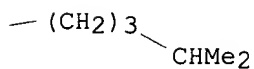
CMF C48 H98 N8

Absolute stereochemistry.

PAGE 1-A



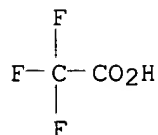
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



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 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:340122

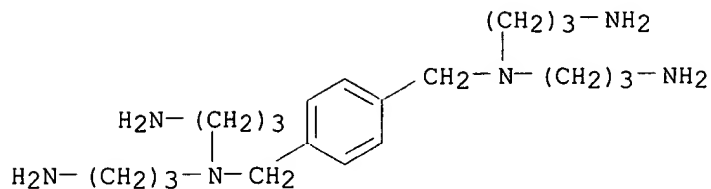
L120 ANSWER 30 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 189076-31-1 REGISTRY

CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA  
 INDEX NAME)

FS 3D CONCORD

MF C20 H40 N6  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223  
 REFERENCE 2: 131:307091  
 REFERENCE 3: 126:293343

L120 ANSWER 31 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 184895-97-4 REGISTRY

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, [S-(R\*,R\*)]-

FS STEREOSEARCH

MF C26 H60 N10 O2 S2

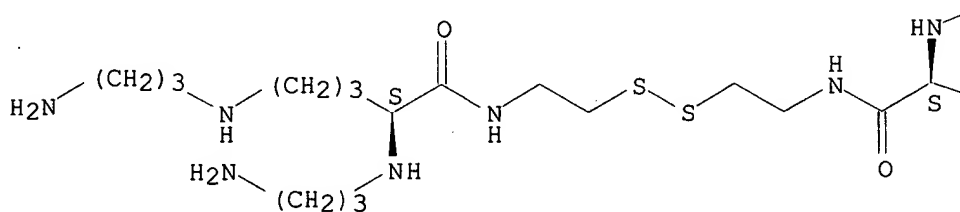
CI COM

SR CA

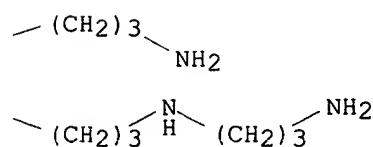
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

REFERENCE 2: 126:42328

L120 ANSWER 32 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 179075-09-3 REGISTRY

CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-  
[[ (4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI)  
(CA INDEX NAME)

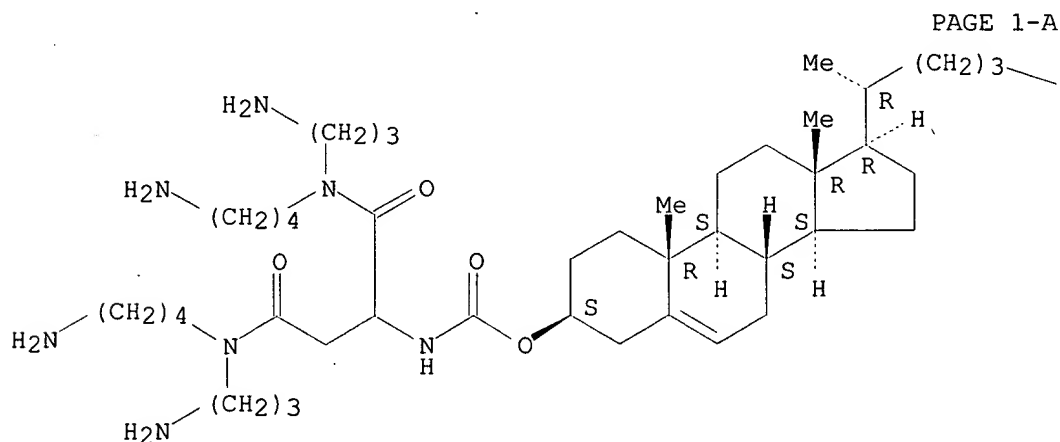
FS STEREOSEARCH

MF C46 H85 N7 O4

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LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PAGE 1-B

 $\sim \text{CHMe}_2$ 

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:8571

REFERENCE 2: 125:107063

L120 ANSWER 33 OF 37    REGISTRY    COPYRIGHT 2002 ACS

RN 148740-50-5 REGISTRY

4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,8,13,17-tetrakis(3-aminopropyl)-  
(9CI) (CA INDEX NAME)

OTHER NAMES:

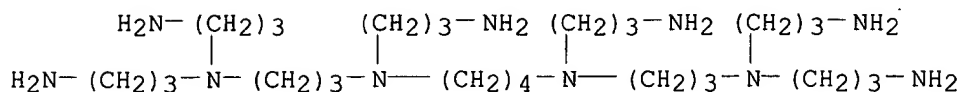
CN NPS 381

FS 3D CONCORD

MF C28 H68 N10



SR CA  
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1967 TO DATE)  
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:45937  
REFERENCE 2: 132:203164  
REFERENCE 3: 132:88193  
REFERENCE 4: 130:119576  
REFERENCE 5: 129:49631  
REFERENCE 6: 128:30379  
REFERENCE 7: 122:1057  
REFERENCE 8: 119:63054

L120 ANSWER 34 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 148717-51-5 REGISTRY

CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,17-bis(3-aminopropyl)- (9CI)  
(CA INDEX NAME)

OTHER NAMES:

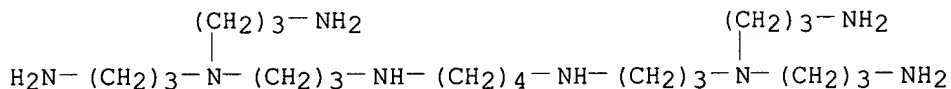
CN NPS 382

FS 3D CONCORD

MF C22 H54 N8

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1967 TO DATE)  
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:203164  
REFERENCE 2: 132:88193  
REFERENCE 3: 130:119576  
REFERENCE 4: 129:49631  
REFERENCE 5: 128:30379

REFERENCE 6: 122:1057

REFERENCE 7: 119:63054

L120 ANSWER 35 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 137946-03-3 REGISTRY

CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis- (9CI) (CA INDEX NAME)

FS 3D CONCORD

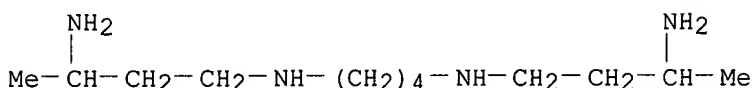
MF C12 H30 N4

CI COM

SR CA

LC STN Files: BEILSTEIN\*, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER,  
USPATFULL

(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:73053

REFERENCE 2: 134:237682

REFERENCE 3: 133:164201

REFERENCE 4: 130:153469

REFERENCE 5: 123:252414

REFERENCE 6: 121:227393

REFERENCE 7: 116:105949

L120 ANSWER 36 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 137945-94-9 REGISTRY

CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis-, tetrahydrochloride (9CI)  
(CA INDEX NAME)

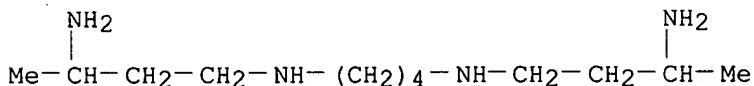
MF C12 H30 N4 . 4 Cl H

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS

(\*File contains numerically searchable property data)

CRN (137946-03-3)



4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)

## 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:105949

L120 ANSWER 37 OF 37 REGISTRY COPYRIGHT 2002 ACS

RN 101394-77-8 REGISTRY

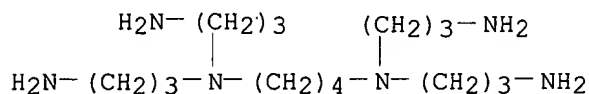
CN 1,4-Butanediamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride  
(9CI) (CA INDEX NAME)

MF C16 H40 N6 . 6 Cl H

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CRN (120239-63-6)



●6 HCl

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

REFERENCE 2: 104:179019

=&gt; d sta que 137

L30 SCR 1598

L31 SCR 1597 AND 1592

L32 SCR 1593

L34 STR

G1-Ak-N-Ak-NH-Ak-G1	NH-G2
1 2 3 4 5 6 7	08 9

VAR G1=NH2/8

VAR G2=ME/ET/I-PR/N-PR

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 3

CONNECT IS M1 RC AT 4

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M3 C AT 2

ECOUNT IS M3 C AT 6

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L37 943 SEA FILE=REGISTRY CSS FUL L34 AND (L30 OR L31) AND L32

100.0% PROCESSED 210556 ITERATIONS

943 ANSWERS

SEARCH TIME: 00.00.12

=> d sta que 185

L69 STR

NH—G2	G1—G3—N—G3—G1	G1—G3—N—G3—G1
@8 9	1 2 3 4 5	14 13 12 11 10

VAR G1=NH2/8

VAR G2=ME/ET/I-PR/N-PR

REP G3=(3-4) C

NODE ATTRIBUTES:

CONNECT IS M3 RC AT 3

CONNECT IS M3 RC AT 12

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L76 SCR 1598

L77 SCR 963 OR 1398

L79 SCR 1569

L82 SCR 1597

L83 SCR 1568

L85 142 SEA FILE=REGISTRY SSS FUL L69 AND (L79 OR (L83 AND L82 AND L77) OR (L76 AND L77))

100.0% PROCESSED 236943 ITERATIONS

142 ANSWERS

SEARCH TIME: 00.00.10

=> d his

(FILE 'HOME' ENTERED AT 08:08:40 ON 01 JUL 2002)

SET COST OFF

FILE 'HCAPLUS' ENTERED AT 08:09:41 ON 01 JUL 2002

E WO98-US7806/AP, PRN

L1 1 S E3, E4

E POULIN R/AU

L2 60 S E3, E6

E AUDETTE M/AU

L3 34 S E3, E4

E CHAREST/AU

L4 6 S E21, E22

L5 1 S E55

E GAUDREALT/AU

L6 25 S (POLYAMINE OR POLY AMINE) AND L2-L5

L7 19 S AMINE#/CW AND L2-L5

L8 25 S L6, L7

L9 14 S BIOLOGICAL TRANSPORT+NT/CT AND L8

E BIOLOGICAL TRANSPORT/CT

E E3+ALL

E E60+ALL

L10 0 S E1+NT AND L8

L11 14 S L1, L9

L12 11 S L8 NOT L11

L13 24 S L11, L12 NOT L1

L14 1 S L8, L11, L12 NOT L13

SEL RN

FILE 'REGISTRY' ENTERED AT 08:13:56 ON 01 JUL 2002

L15 34 S E1-E34  
L16 STR  
L17 50 S L16  
L18 STR L16  
L19 0 S L18  
L20 STR L18  
L21 0 S L20  
L22 STR L20  
L23 0 S L22  
L24 SCR 2043  
L25 0 S L22 NOT L24 SAM  
L26 STR L18  
L27 0 S L26  
L28 STR L26  
L29 0 S L28 CSS SAM  
L30 SCR 1598  
L31 SCR 1597 AND 1592  
L32 SCR 1593  
L33 2 S L28 AND (L30 OR L31) AND L32 CSS  
L34 STR L18  
L35 2 S L34 AND (L30 OR L31) AND L32 CSS SAM  
L36 0 S L34 AND L32 CSS  
L37 943 S L34 AND (L30 OR L31) AND L32 CSS FUL  
SAV L37 KUMAR529/A  
L38 STR L34  
L39 2 S L38 CSS SAM SUB=L37  
L40 4 S L38 CSS FUL SUB=L37  
SAV L40 KUMAR529A/A  
L41 STR L34  
L42 32 S L41 CSS SAM SUB=L37  
L43 752 S L41 CSS FUL SUB=L37  
SAV L43 KUMAR529B/A  
L44 STR L41  
L45 0 S L44 CSS SAM SUB=L43  
L46 19 S L44 CSS FUL SUB=L43  
SAV L46 KUMAR529C/A  
L47 STR L44  
L48 0 S L47 CSS SAM SUB=L37  
L49 2 S L47 CSS FUL SUB=L37  
SAV L49 KUMAR529D/A  
L50 STR L47  
L51 0 S L50 CSS SAM SUB=L37  
L52 0 S L50 CSS FUL SUB=L37  
SAV L52 KUMAR529E/A  
L53 STR  
L54 2 S L53 SAM SUB=L37  
L55 4 S L53 FUL SUB=L37  
SAV L55 KUMAR529F/A  
L56 14 S L15 AND L37  
L57 6 S L56 AND 10/N NOT C26H46N1004S  
L58 20 S L15 NOT L56  
L59 2 S L58 AND (C20H40N6 OR C18H44N6S2)  
L60 8 S L57, L59  
L61 STR L34  
L62 0 S L61 CSS  
L63 STR L61  
L64 0 S L63 CSS  
L65 SCR 1996 AND 1593  
L66 1 S L63 AND L65 CSS  
L67 SCR 2043 OR 2039 OR 2050 OR 2049 OR 2053 OR 2052 OR 2051 OR 205  
L68 0 S L63 AND L65 NOT L67 CSS  
L69 STR L63

L70 0 S L69 SAM  
 L71 0 S L69 AND L65 NOT L67 SAM  
 L72 SCR 2127  
 L73 0 S L69 AND L65 NOT (L67 OR L72) SAM  
 L74 SCR 1562  
 L75 SCR 1568 AND 1597  
 L76 SCR 1598  
 L77 SCR 963 OR 1398  
 L78 0 S L69 AND (L74 OR (L77 AND (L76 OR L75)))  
 L79 SCR 1569  
 L80 0 S L69 AND (L79 OR (L77 AND (L76 OR L75)))  
 L81 SCR 1595  
 L82 SCR 1597  
 L83 SCR 1568  
 L84 0 S L69 AND (L79 OR (L83 AND L82 AND L77) OR (L76 AND L77))  
 L85 142 S L69 AND (L79 OR (L83 AND L82 AND L77) OR (L76 AND L77)) FUL  
 SAV L85 KUMAR529G/A  
 L86 9 S L69 CSS SAM SUB=L85  
 L87 SCR 2039 OR 2040  
 L88 0 S L69 NOT L87 CSS SAM SUB=L84  
 L89 SCR 2039  
 L90 9 S L69 NOT L89 CSS SAM SUB=L85  
 L91 SCR 2040  
 L92 6 S L69 NOT L91 CSS SAM SUB=L85  
 L93 3 S L90 NOT L92  
 L94 112 S L69 NOT L91 CSS FUL SUB=L85  
 SAV L94 KUMAR529H/A  
 L95 4 S L53 FUL SUB=L94  
 SAV L95 KUMAR529I/A  
 L96 108 S L94 NOT L95  
 L97 2 S L15 AND L85  
 L98 8 S L60, L97  
 L99 11 S L95, L98  
 L100 137 S L40, L46, L49, L95, L99, L60, L96

FILE 'HCAPLUS' ENTERED AT 11:22:27 ON 01 JUL 2002

L101 193 S L100  
 L102 5 S L1-L5 AND L101  
 L103 120 S L101 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)  
 L104 10 S L103 AND BIOLOGICAL TRANSPORT+NT/CT  
 E BIOLOGICAL TRANSPORT+ALL/CT  
 E E60+ALL  
 L105 0 S E1+NT AND L103  
 L106 64 S L103 AND (POLYAMINE OR POLY AMINE OR AMINE#/CW(L) POLY)  
 L107 10 S L106 AND TRANSPORT?  
 L108 82 S L100(L) (THU OR BAC OR BIOL OR USES)/RL  
 L109 58 S L108 AND L103  
 L110 9 S L109 AND L104  
 L111 11 S L109 AND TRANSPORT?  
 L112 0 S L109 AND SIGNAL?(L) TRANSDUC?  
 L113 15 S L102, L104, L110, L111  
 L114 13 S L113 NOT CDNA/TI  
 L115 10 S L103 AND 63/SC, SX  
 L116 15 S L114, L115  
 L117 5 S L116 AND TRANSPORT?(L) INHIBIT?  
 L118 10 S L106 AND L116  
 L119 15 S L116-L118  
 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 11:29:42 ON 01 JUL 2002

L120 37 S E1-E37

FILE 'REGISTRY' ENTERED AT 11:30:47 ON 01 JUL 2002

FILE 'HCAPLUS' ENTERED AT 11:31:47 ON 01 JUL 2002

FILE 'REGISTRY' ENTERED AT 11:32:35 ON 01 JUL 2002